보건학 박사학위 논문

The effect of predator species richness on rodent-borne disease emergence and incidence

포식동물 종 풍부도가 설치류매개 감염병 출현과 발생에 미치는 영향

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Abstract

The effect of predator species richness on rodent-borne disease emergence and incidence

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Rodents account for about 40% of all terrestrial mammals and distributed throughout the world as the one of the most flourished species. They are mainly located in the lower level in the hierarchy of food web and are in the important positions to maintain the structure of the biotic ecosystem. Due to their excellent adaptability to the various environment, they are prevalent even in the area of human residence. Because of these characteristics, it is a host of pathogens that cause human infectious diseases and has been a threat of public health, historically (e.g., the Black Death in the Middle Ages). Even recently, rodent-borne diseases (RBD) have caused

various public health and socioeconomic burden, ranging from emerging / re-emerging infectious diseases such as Lassa fever and Black Death to endemic diseases, such as hantavirosis. Disaster-related diseases such as leptospirosis also have been a public health concerns. Many studies have been implemented to identify risk factors of the RBDs which can be applied to develop practical interventions and to predict risk area. However, most studies have focused on individual-level factors, socio-demographic factors, or abiotic environmental factors, such as climate and geographical factors, and relatively ignored the role of biotic factors, especially predators.

Intuitively thinking, the relationship between predators and the reservoir rodents would be simple; The presence of predator suppress the rodent population whereas the absence increase them. The simple intuition would be acceptable for the short-term, but in terms of long-term situation, things become complicated. In the presence of predators, especially specialist predators, the population of prey species decreases in the short term, but the decreased population size of prey suppress the predator population by lack of food, subsequently drive population expansion of prey species. Ostfeld et al., one of the prominent figures in disease ecology, suggested that generalist predators would be a key regulator of prey population and chronically suppress the population, as their predation pressures are diversified not focusing on a single species.

In this study, I investigated whether the species richness of predator directly affects the emergence and incidence of RBDs in human population. To generalize the

findings to overall global scale, the relationships through three different empirical studies involving various ecological contexts, different diseases, and heterogeneous distribution level of wildlife were investigated (Table A-1).

The first study was about the Lassa fever in West Africa. I targeted the area without Lassa fever outbreak until 2006, and compare the predator species richness in the area with Lassa fever outbreak after 2006 to the other areas without reported events, in order to examine the regulatory role of predator species richness on the geographical expansion of Lassa fever. The results showed that the risk of Lassa fever emergence was lower in areas with high species richness of rodents than those with lower species richness (Table A-2).

The second study was for the New World hantavirosis (hantavirus pulmonary syndrome) in Brazil. The objective of the study was finding the association between diurnal predator species richness and probability of hantavirosis occurrence in the municipalities between 2007 and 2014. The results showed that the probability of occurrence of reported hantavirus infections was lower in areas with higher species richness of diurnal predatory specie. On the other hand, in areas with high species richness of nocturnal predators, the probability was higher than the others (Table A-2).

In the third study, the number of cases for endemic hemorrhagic fever with renal syndrome (HFRS) was targeted to examine the association with species richness of diurnal predators with surveillance data from Korea Center for Disease Control. The results showed that the relative risk of HFRS was higher in areas with high

species richness of diurnal predators, and no significant association was found with species abundance of nocturnal predators (Table A-2).

Although each study has several limitations, and the interpretation should be careful as ecological studies using open access data. However, the study results showed that the significant negative association between RBDs and species richness of predators in the same circadian rhythm with reservoir rodents, when the reservoir rodents were dominant species in the regions, such as Brazil and Korea. The findings strongly support the hypothesis, proposed at the beginning of this study, that the species richness of predators has a noticeable modulating effect on RBDs in human population. Although the effect size of association presented in this study is not high, the implication of the study was not limited to the diseases employed in this study, rather can provide a possible explanation of all other RBDs. Furthermore, the study results may support the necessity of wildlife conservation in a utilitarian point of view.

Keywords: Predator, Species richness, Rodent-borne diseases, Emerging infectious diseases, One Health

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Table A-1. Study designs

Categories	Chapter 2	Chapter 3	Chapter 4
Study area	West Africa	Brazil	South Korea
Wildlife diversity	High	High	Low
Disease	Lassa fever	Hantavirosis	Hemorrhagic fever with renal syndrome
Outcome measurement	Whether the disease has been emerged (y/n)	Notification of one case or more in the municipality during the period 2007-2014 (y/n)	The number of cases
Time covered	2006 – 2017	2007 – 2014	2006 – 2016
Unit (N)	One-degree grid (N = 191)	Municipality (N=5,563)	Sigungu (N = 201 x 11)

Table A-2. Result comparison

Species richness	**Relative risk (95% CI, final model*)**		
	Chapter 2	Chapter 3	Chapter 4
Rodents	**0.909 (0.850 – 0.972)**	**0.906 (0.878 – 0.934)**	1.071 (0.997 – 1.150)
Predators (same circadian rhythm)	1.074 (0.919 – 1.255)	**0.949 (0.907 – 0.993)**	**0.899 (0.826 – 0.975)**
Predators (different circadian rhythm)	1.061 (0.994 – 1.133)	**1.371 (1.258 – 1.499)**	0.995 (0.841 – 1.181)

*Final model: Multivariable analysis including all species richness variables adjusted by anthropogenic, climate, forest, land cover, geographic factors

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Neglected, but

plausible effects of predator species richness on rodent-borne diseases

1.1. Impact of rodent-borne diseases

Due to extensive development of antimicrobials and vaccines, many infectious diseases have been considered to be under control. For example, small pox, the disastrous pathogens previously, has been eradicated, and polio incidence has remarkably reduced recently. However, it is still a struggle to combat with some infectious diseases that originated from out-of-human wildlife population, called zoonotic diseases (or zoonoses), mainly because the source of infection cannot be eradicated, and our understanding of such diseases including their transmission dynamics is still not clear.

Rodent-borne disease (RBD) is the one of examples of the zoonoses. RBD has 66 diseases caused by viral, bacterial and parasitic pathogen, such as Lassa fever, Hantavirosis, leptospirosis, etc. (Table 1-1), and 217 rodent species have been known as the reservoirs of the diseases (1). Considering that species in Order Rodentia are the most abundant mammals on the planet (2) and widely distributed including human dwellings (cultivated or urban area), the risk of transmission of pathogens from Rodentia species to human population, so called cross-species spillover (3), is relatively higher than other mammals. In this regards, the RBD have been one of the most important public health concern historically.

Even now, the concerns have been persistent and even increased. Recently in Nigeria, unprecedented outbreak of Lassa fever, followed by Eloba epidemic, caused severe economic and social dislocation (4, 5), and Plague has also been reemerged in various regions including Madagascar (6). Besides these diseases

dominating headlines, endemic RBDs such as hemorrhagic fever with renal syndrome (HFRS), and food-related RBDs, such as salmonellosis have steadily deteriorated local public health.

Furthermore, the impact of RBDs have been expected to increase in the future. As rodent species are ecologically generalists (1, 7, 8), indicating their resilience to the impact of anthropogenic modification of habitat, it is difficult to limit the population by interventions. Considering that the anthropogenic pressure could facilitate the ecological homogenization, the situation that only resilient species has survived, the contact rate between human and rodents and the chance of spillover event would increase. However recent studies on zoonosis epidemiology tend to focus more on bat-borne or suspected bat related diseases, represented by Ebola, Hendra, Nipah, and SARS etc., than RBDs (9, 10), although the number of pathogens is higher in rodents than bats (11).

Table 1-1. List of Rodent-borne diseases

Diseases	Agents	Vector needed
Hantavirus pulmonary syndrome	V, Bunyaviridae	No
Hemorrhagic fever with renal syndrome	V, Bunyaviridae	No
Lassa fever	V, Arenaviridae	No
Leptospirosis	B, Spirochaetes	Yes
Lyme disease	B, Spirochaetes	Yes
Leishmaniasis	P, Zoomastigophorea	Yes

Agents: V, B, and P indicate virus, bacteria and parasite, respectively

Vector needed: whether vectors (such as ticks and mosquitos) are needed to spillover the pathogen from rodents to human

The list is not comprehensive and reorganized from (7, 10)

1.2. Previous studies on risk factors of rodent borne diseases

The social impact and economic burden of RBDs have galvanized epidemiological studies to find out risk factors or determinants which enabled to develop intervention strategies or to predict areas in risk. So far, these approaches mainly focused on human related factors, such as socio-demographic and economic factors, or environmental drivers, related to geography, land use, and climate, etc.

Iles et al (12) reported that socio-economic levels of local residents were associated with chance of contact with rodents, their knowledge, attitude and behavior of rodent borne diseases. They showed that the improvement of socio-economic status also improved capacities on preventing rodent borne disease. Especially, they found that quality of house construction was related to reducing human-rodent contact frequency.

Prist et al (13) conducted ecological study by analyzing secondary data for Brazil and the results showed that incidence of Hantavirus infection, which is RBD, was positively associated with landuse of sugarcane, regional Human Development Index, and forest land cover. They also provided evidences that temperature can increase the risk, so the climate change in the future could increase the incidence risk in Brazil (14).

A study in Kenya by Young et al (15) suggested that human development pressure that changed forest region to cropland would drive systematic increases in risk of RBDs.

Zeitz et al (16) investigated 494 workers in Arizona and New Mexico, whose occupation has been considered as vulnerable jobs for RBDs, such as farming, national park services, and plumbing etc. Although all the study participants were seronegative results for hantavirus infection, they found that the workers have frequently exposed to risk behaviors for RBD infection.

Besides, similar epidemiological studies have been conducted on other vector-borne diseases (VBDs) as well. Anthropogenic factors (17), such as tourisms, air travel, live animal husbandry (18) were reported as major risk factors. On the other hands, climate and meteorological factors (19) also showed association with the risk.

1.3. The effect of predators' diversity as a remaining question

As discussed in the previous section 1.2., many epidemiological studies focused on socio-economic, geographic, land use and land cover, and climate risk factors. The RBD, however, literally implies the close associations with rodents' ecological characteristics, and this gives inference that factors that related to the ecology of rodent population could affect the risk of RBDs in human population.

Interactions with other rodent species would be related to RBDs in this regards. The existence of other rodent species or species in the similar level of food chains indicates competition of common food source, which influences the reservoir rodents' activities and survival rate. Accordingly, the diversity of rodent species, called host diversity, has been actively studies to investigate their effects on RBDs emergence and incidence. However, there were significant discrepancies in the results of those studies with heterogeneity in the methodologies and study setting. Among the three incompatible theories, amplification effect, dilution effect, and null effect, arguments have still not been concluded.

The first assertion is "amplification effect". Amplification effect indicates the phenomenon that biodiversity richness increases the number of emergence and incidence of diseases in human population. While there are several underlying mechanisms that supporting the effect, majority of studies suggested mechanisms below (Table 1-2): 1) Rich biodiversity cause rich pathogen (pathogen diversity), including zoonotic pathogens, subsequently increasing risk of spillover event, 2) Rich biodiversity may support enough food meals for blood-sucking vectors, causing

increase density of vectors.

Jones et al (20) developed statistical model with global scale, including mammal species diversity, precipitation, latitude, human population growth, and the results showed that significant positive association between mammal species diversity and zoonotic disease emergence. However, the effect size (point estimate of odds ratio) was relatively small, as 1.01.

Although there was no description on spillover events or diseases incidence in human population, Hudson et al (21) suggest that parasites diversity, including pathogenic, tends to be richer where the diversity of host is rich. Similar report has been made in (22), with marine environment.

Murray et al (23) used a model including mammal biodiversity, flight traffic, climate, publications, land area, health expenditure, population size, latitude to explain emergence of all infectious diseases including ZD, and mammal biodiversity showed significant positive association. Dunn (24) reviewed evidences of disservice of nature and stated that rich biodiversity increased risk of human infectious diseases, implying necessity of appropriate manage of nature to prevent the disservice event.

The second stream is “dilution effect”. The dilution effect means that disease incidence and emergence risk will reduce by increased diversity of species, and usually comes from environmentalists to support conservation or

preservation initiatives (25) The suggested mechanisms for this theory by previous studies are as below (Table 1-2): 1) Rich biodiversity indicates higher chance of “dead-end” of transmission chains due to higher density of low-competency hosts, subsequently induced protective effect against spill-over events. 2) Rich biodiversity may reduce the number of vectors because the other non-vector arthropod would compete with vector arthropods.

Keesing et al (26) reviewed both sides about the effect of biodiversity on human infectious diseases and found that the evidence is not enough to make a determinative conclusion. However tentatively concluded that preserving intact ecosystems and their rich biodiversity would reduce the spill over events.

Pongsiri et al (27) reviewed evidences supporting dilution effects and proposed that biodiversity loss followed by host homogenization (situation that only several resilient species survive) could increase the incidence of infectious diseases in human population, by change in host-pathogen contact rates, change in competent host-vector contact rates, change in pathogen prevalence, expansion of range through anthropogenic transport etc

In the recent review article by Ostfeld and Keesing (28) they recite the possible mechanisms of amplification effects and refuted the mechanisms one by one. They found that there is no clear evidence for one important

casual-link that higher diversity of pathogens associated with high diversity of zoonotic pathogens. On the other hands, they suggested substantial evidences that high diversity have protective effect against disease transmission in humans.

Meanwhile, some studies stood for the third theory, the null effect. They contend that the relationship between biodiversity and disease incidence cannot be general, but depends on the idiosyncratic environment in the local community. Salkeld et al (25) conducted a meta-analysis with recent relevant studies to investigate the relationship and suggested that infectious disease transmission risk could depends on local ecological characteristics such as types of composition of reservoir hosts and density of vectors and their overall dynamics, and many studies also support their suggestions for this issues (29-33)

Table 1-2. Suggested explanation of amplification effect and dilution effect for zoonotic diseases and vector-borne diseases in previous studies

	Amplification effect	**Dilution effect**
Suggested mechanism (zoonotic diseases)	Biodiversity richness → Pathogen richness → Zoonotic pathogen richness → Higher chance of spill-over	Biodiversity richness → Higher density of species with low-competency → Higher chance of "dead-end" of transmission chains → Lower chance of spill-over
Suggested mechanism (vector-borne diseases)	Biodiversity richness → Higher density of mammals providing feed for vectors → Higher density of vectors → Higher chance of spill-over	Biodiversity richness → Higher density of non-vector arthropod → Lower density of vectors → Lower chance of spill-over

Details of Scoping review framework and search strategies were described in Appendix

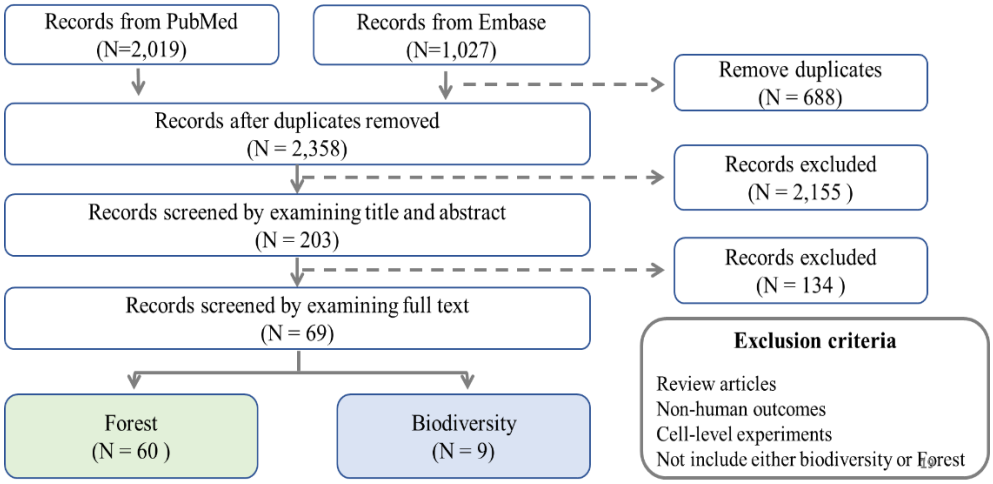

Figure 1-1. Scoping review process

Table 1-3. Studies identified from the scoping review

Author	Year	Disease	Host	Association
Ezenwa et al	2006	WN	Avian	Negative
LoGuidice et al	2008	Lyme	Small mammals	NS
Suzan et al	2008	Hanta	Small mammals	Negative
Allan et al	2009	WN	Avian	Negative
Derne et al	2011	Lepto	Mammals	Negative
Werden et al	2014	Lyme	Small mammals	Idiosyncratic
Myterud et al	2016	Lyme	Deers	Positive
Levine et al	2017	WN	Avian	Positive
Walsh et al	2017	RVF	Mammals	Positive

In addition to the interactions with other rodent species, predation pressures could independently modify the behaviors and survivals of reservoir rodents. Intuitively, the existence of predators would suppress the rodent population, subsequently, the contact frequency between human and the rodents would decrease. However, Ostfeld and Holt (34) suggested that the causal link of predators on rodent population and the consequent RBD incidence in human population is not that simple. To explain, although the presence of predators suppresses the population density of rodents in the short-tem, the long-term average population density would not be changed due to decreased food source of predators followed by decreased population (Figure 1-2). This is why the previous field experimental studies that artificially excluded specific predators did not show significant differences in rodent populations (35). A feral rabbit problem in Australia is another example.

Although the effect of simple presence of predators on rodent population dynamics is questionable, the link between diversity of predators and rodent population could be plausible. Embar et al (36) found that gerbils foraging efforts were less active when more various types of predators were presented. A review study (37) also reported that multiple researches supported that species richness of predators could suppress prey population and reductions in predator richness can increase prey density.

These findings were consistent with the results of recent studies in disease ecology that predator richness was associated to prevalence in natural host. Orrock et al (38) investigated prevalence of Sin Nombre virus in the eight California Channel Islands and found that islands with higher species richness of predators showed less prevalence among deer mice. A recent study by Ostfeld et al (39) suggested that diverse predator functionality could reduce the prevalence of Lyme disease in vectors.

However, the protective effect of predator richness on RBDs in human population was not conclusive. Although the Ostfeld study (39) employed well designed, respectful experiment, they focused on tick-borne disease and the dynamics in RBDs could be different. In terms of study by Orrock et al (38), they targeted RBDs, but the sample size in the association analysis was too small (n = 8) and ecologic characteristics in island could be distinctive which is difficult to be generalized. Moreover, the association with RBD incidence in human population would be different than prevalence in rodents, and it could have more practical and direct implication in public health perspective.

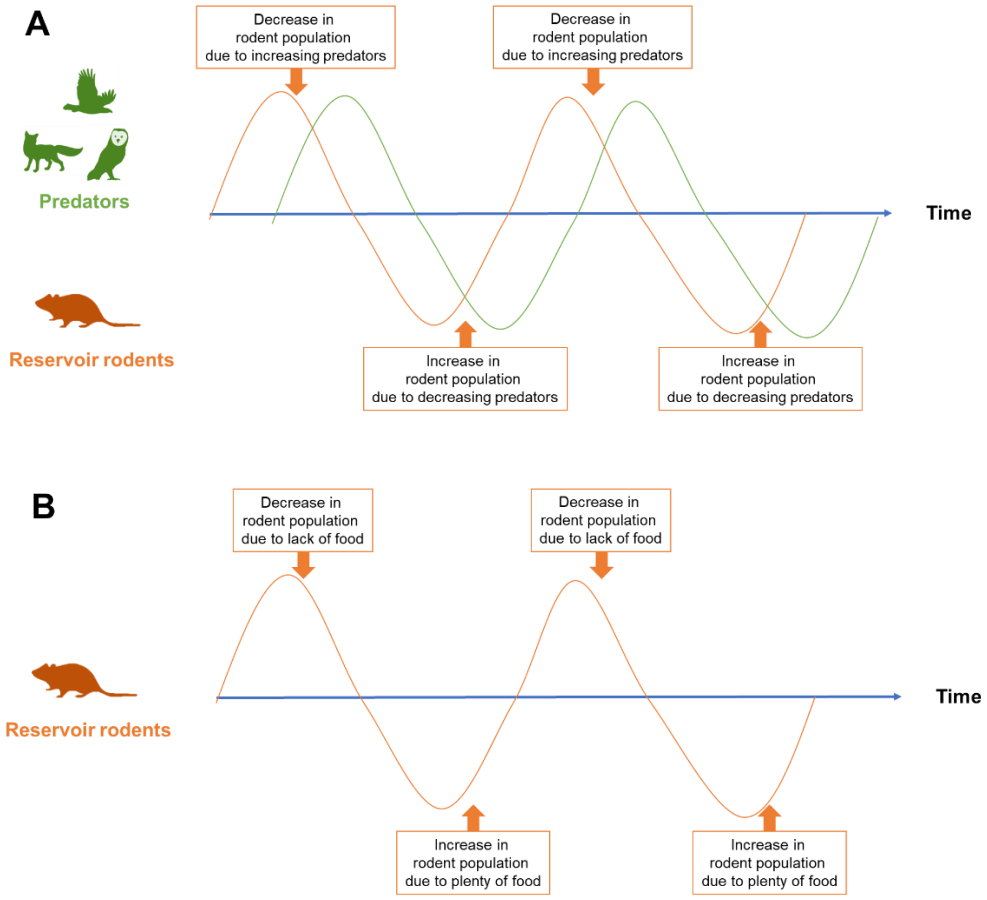

Figure 1-2. The effect of existence of predators on rodent abundance proposed by Ostfeld and Holt (34)

1.4. Species richness as the most pragmatic approaches to explore the association of predators' diversity with rodent-borne diseases

Various indicators would be applicable to measure the "biotic" (wildlife) factors in the epidemiological studies, and density and diversity are the two major indicators (or groups of indicators) which are the most intuitive and simplest ones that have been widely used.

The density considered the number of population in given area. The concept is exactly same as human population density, and it enables to explain directly on the effects of wildlife. For example, assuming that there are current and previous density data of reservoir rodents, we could investigate the association of some RBDs and the density and the interpretation would be direct and intuitive. Due to this strength, many studies described in the previous section incorporated the density indicators usually in the field experimental settings. However, the density indicator is relatively difficult to measure in many cases, and sometimes impossible, although there are some established methodologies, such as capture-recapture method (40). Therefore, it could be applicable in the relatively small area or experimental settings, but adopting the approaches on researches of which study area is large scale could be extremely difficult. In some cases, the probability of occurrence (by ecological niche modelling) have been used, to make similar implication as population density, but the meaning and interpretation cannot be the same.

The diversity, on the other hands, focused on the number of class of certain biota in a given area, such as number of genera, or species. Specifically, there are two

categories in the indicator group; richness and evenness. Richness (or species richness) only represents the number of species, whereas evenness is incorporated with the number of population of each species. For example, supposing that there are 8 rats, 1 cats and 1 dogs in area A, and 4 rats, 3 cats and 3 dogs in area B, area A and B show same species richness as 3 (indicating there are 3 species; rats, cats and dogs) but the evenness is higher in B (indicating that the composition is more even in area B). While the diversity should be described by both species richness and evenness, evenness could be better and sophisticated indicator because of its weight on population. However, similar with density indicators, it is relatively more difficult to measure, and even more difficult than density, because it should count entire species population rather than just a species of interest.

In comparison to density and evenness indicators, species richness could be relatively easy to obtained and evaluated. When it comes to large scale study area; national level or global level, species richness is almost only practical measurement at this moment. For example, Jones et al (20) and Allen et al (41) have used mammalian species richness in their global level studies as an explanatory factor or predictor for recent infectious disease emergences.

1. 5. Study framework and main objectives

Main study objective that I would like to pursue throughout this dissertation is developing a generalized theory that elaborate the effect of predator species richness on RBDs emergence and incidence which can be applied in ecologically various environment. To this ends, diverse study areas, both biodiversity-rich areas, and poor have been included, and also both emergence and incidence events has been incorporated (Table 1-4).

Specifically, I examined the two hypotheses which are the main objectives described as below:

Hypothesis 1. The higher predators' species richness would decrease the risk of rodent-borne emergence and incidence in human

This is the main hypothesis of the study, and the basic idea was developed from the theory suggested by Ostfeld et al in 2004 (34). They proposed that generalist predators may chronically suppress the fluctuation of rodent population by avoid to focus the predation pressure on a single species. With the similar mechanism, I hypothesized that diverse predator's preference on preys, represented by predator's species richness, could suppress the fluctuation of rodent population, which may prevent or hinder the spill-over event between rodent and human. Although previous studies dealt with the hypothesis by examining the association between disease prevalence in rodent population and predator richness (38) or with tick-borne diseases

(39), the direct association between RBDs and predator species richness was not reported yet and a recent review study also pointed that it has been neglected (42).

Hypothesis 2. The higher number of rodent species may decrease the risk of rodent-borne disease in human

The hypothesis was called “dilution effect”. Although large volume of studies already dealt with the issue, and mainly supported the effect (26-28, 43-45), the arguments is still ongoing (25, 46) as described the previous section. The hypothesis is not the main topic in this study, but I expected the study results would supplement the current debate on dilution effect.

In this study, the target diseases were restricted as Lassa fever and hantavirosis (both new world hantavirosis, hantavirus pulmonary symdrome (HPS) and old world hantavirosis, hemorrhagic fever with renal syndrome (HFRS)), since the range of reservoir species is relatively not broad, and additional vectors, such as mite, mosquitos and food, that would be needed to occur spill over, are not necessary for those two disease. Besides, although Lassa fever can be spread via human to human transmission, the route is usually limited and only occasionally happened in nosocomial environment, subsequently we can concentrate on the effect of natural environmental factors and simplified the study results and interpretation.

To adjust confounding factors in the association between predator species richness and RBDs emergence and incidence, I included covariates that have been studied as associated with both wildlife and RBDs, including socio-demographic factors, economic factors, deforestation (47, 48), geographic factors (49), land cover (50), climate factors (51) (Figure 1-3).

Also, investigating the impact of the wildlife biodiversity on RBDs would be significant for the practical aspects, such as developing interventions. For example, effective implementation of RBDs control strategies needs prioritization of time and places (i.e. risk area (hot spots), and risk period), and risk factors should be identified to determine the risk area and period.

Meanwhile this study may imply expansion of conventional public health studies into convergence studies with other "non-human" disciplines, in this case ecology. Especially in Korea, as the outcome of interest in public health field is human health, many studies focus on "human" or "social" related factors to explain the outcomes (by using human and social related independent variables in the models). However, for some phenomenon, such as spreading of RBDs that include non-human environment aspects, this approach is not enough to fully explain it. This study would have a role to fill this gap, and expand the perspective of public health studies by incorporating non-human side.

Table 1-4. Comparison of research design across three following chapters.

	Chapter 2	Chapter 3	Chapter 4
Study area	West Africa	Brazil	Korea
Wildlife diversity	High	High	Low
Outcome measurement	Whether the outbreak has been expanded (y/n)	Notification of one case or more in the municipality during the period 2007-2014 (y/n)	The number of incidence
Disease	Lassa fever	Hantavirosis	Hemorrhagic fever with renal syndrome
Time covered (disease)	2006 – 2017	2007 – 2014	2006 – 2016
Assessment period for wildlife	2006 - 2017	2002 -2017	2006 - 2013
Unit (N)	One-degree grid (N = 191)	Municipality (N=5563)	Sigungu (N = 250 x 11)

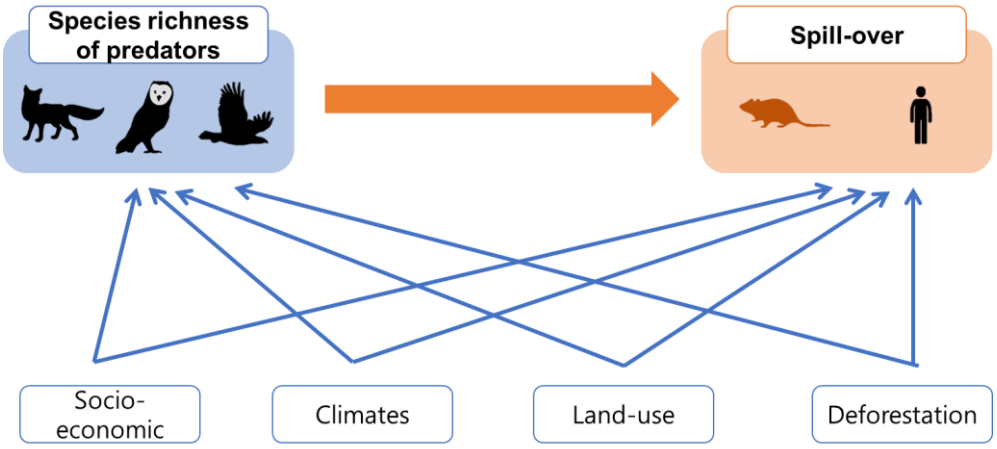

Figure 1-3. The main explanatory variable and covariates incorporated throughout this study, represented by directed acyclic graph

Chapter II.

Species richness of rodents as a potential limiting factor for the geographical expansion of Lassa fever in Western Africa

2. 1. Introduction

2.1.1. Local and global impact of Lassa fever

Lassa fever is an acute viral hemorrhagic fever, and a RBD, transmitted from *Mastomys natalensis*, a multi-mammate rat, broadly distributed across sub-Saharan Africa. The disease burden is not well known but the annual infection cases have been estimated as 100,000 to 300,000 with 5,000 mortality cases (52) which is extrapolated from a longitudinal study (53). Recently, the number of cases surged in Nigeria in 2018 (5), and the unprecedented outbreak caused severe social and economic dislocation at the national level.

In addition to this local impact, Lassa fever has also been a global concern due to the imported cases from West Africa to Europe, including Germany (54) and UK (55) or other regions, such as US (56). Considering its relatively long incubation period (6 to 21 days (57)) and global increase of air transportation, the risk of disease importation is persistent.

2.1.2. Geographical limitation of Lassa fever outbreak

In the rest of sub Saharan Africa, except for Western Africa, there has been no report for autochthonous infection of Lassa fever. While it is a great fortune, it is also an interesting phenomenon in the viewpoint of disease ecology. Considering that ancestral origin of Lassa virus rooted from 1,000 years ago in Nigeria, and only recently spread to the western regions called Mano River union (MRU), including

Cote d'Ivoire, Guinea, Liberia and Sierra Leone (58), it is strongly suspected that there should be limiting factors that hindered the expansion of disease outbreak and caused the difference between regions.

Geographical barriers have been considered as the possible explanation. Siddle et al (59) found that genetic variation of Lassa virus was affected by geographical features, such as rivers, and suggested that the geographical barriers would suppress migration of reservoir rodents. Another example is a mountain chain between Nigeria and Cameroon which could be a reason why there was no Lassa emergence in Cameroon, while Nigeria suffered large-scale outbreak. However, these would not be enough to account for the absence of Lassa fever in some part of Western Africa. If the geographical distribution of Lassa fever were attributed only to the physical barriers, the relatively lower cases in countries between MRU and Nigeria would not be explainable. Meanwhile, a recent study (60) suggested co-evolution hypothesis that explains the absence of Lassa fever in a certain region by genetic difference of reservoir rodents. However, the explanation has been rebutted because host range of Lassa fever virus is relatively broad (61).

Biotic structures, i.e., food web structure, would also be a possible candidate to elucidate the geographic limitation of Lassa fever. Jones et al (20) showed that the mammalian species richness could increase the risk of disease emergence, but, on the other hands, Ostfeld et al proposed dilution effects that the diversity of host mammals (i.e. diversity of rodent species) could protect the spill over event in specific conditions (45). The role of predators was also discussed previously (34) and recent

studies revealed the association with empirical evidences (38, 39), but the direct association between factors associated with predators and disease emergence in human population has not been shown.

2.1.3. Goal of study and study design

Throughout this study, the association between wildlife species richness and the risk of geographic expansion of Lassa fever was investigated. Considering that the available species distribution data, which were used to calculate species richness, was updated between 2006 and 2017, the target outcome was set as Lassa emergence in the same period (from 2006 to 2017). To this end, the history of Lassa fever outbreak was divided by before 2006 (up to 2005) and after (i.e., 2006 – 2017), and excluded the outbreak area before 2006. Then, the predator species richness of newly Lassa fever-emerged area was compared to that of the other areas (Figure 2-1).

In terms of species richness, three variables were incorporated as the major explanatory factors; rodent species richness, nocturnal predator species richness and non-nocturnal predator species richness. The rodent species richness was included to investigate whether the dilution effect works for Lassa fever emergence prevention, and the predator species richness was incorporated to examine the suppression effect of predators on the spill-over event. Considering that the major reservoir species of Lassa fever is nocturnal, the effect of nocturnal predators and non-nocturnal predators were discretely tested. In addition, species which were under threat of extinction were

not included in the main analysis, because species with relatively lower population would not be influential enough. To this end, species categorized as “Least Concern (LC)” or “Near threatened (NT)” by IUCN (62) were included and the others (“Vulnerable (VN)”, “Endangered (EN)”, “Critically Endangered (CR)”) were excluded in this study.

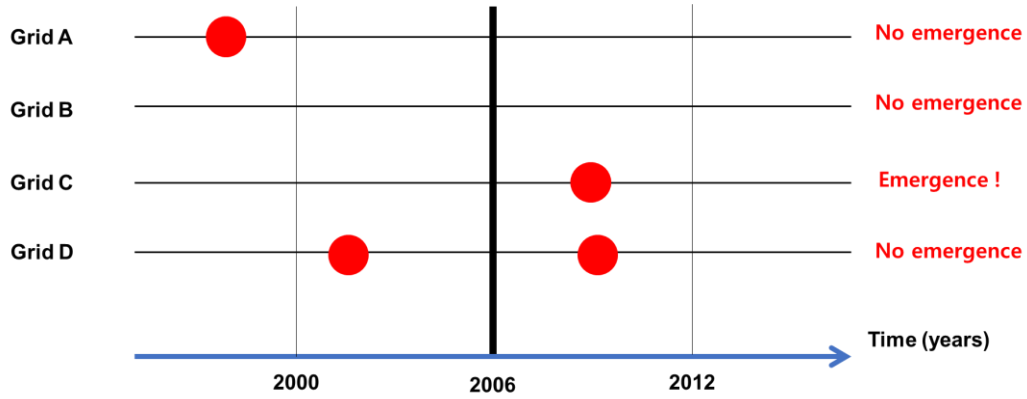

Figure 2-1. Categorization of the study regions in this chapter
Note: In this study, the outcome of interest was Lassa emergence event after 2006. To this end, the regions with Lassa reported case before 2005 was excluded and compared regions which suffered Lassa emergence after 2006 to regions without any Lassa cases. The figure illustrated all possible types of study area category in this study. the grid A and D represented regions with Lassa cases before 2005 and excluded in the analysis. Grid C indicated the area with newly Lassa emergence after 2006 and the species richness of Grid C was compared to that of Grid B in this study.

2.2. Materials and methods

2.2.1. Data acquisition

To examine the study hypothesis, various types of data representing Lassa fever outbreak (main outcome), species richness of wildlife (main explanatory variables), and other covariates, including socio-demographic, climate, land cover, and geographic factors, were needed. Although there was no systematic data collection that covered all of these variables, the feature of spatial data that can be merged based on common spatial attributes, enables to comprehensively utilize a number of data from various sources (Table 2-1).

2.2.1.1. Lassa fever outbreak

Each country in Western Africa, has developed national level surveillance system for infectious diseases, but the sensitivity and specificity of data are highly heterogeneous. Consequently, depending solely on national surveillance data would occur systematic measurement bias.

Web-based surveillance data was considered in this regards. Although it is not an official report, and sometimes contains false-positive report (especially when the source of data is news media), various studies have employed the web based data to investigate epidemiological research questions (63, 64) and even to evaluate infectious diseases detection capacity (65). It implies that the web-based surveillance would be the best possible measurements.

In this study, ProMED-Mail (66), Health map (67, 68), World Health Organization Disease Outbreak News (WHO DONs) (69) were used to find regions with Lassa fever outbreak. ProMED-mail is an expert-supervised system that includes both human and animal outbreak information obtained from reports of national level authorities (both official report and interpersonal communication), international organization and local news articles. The database is fully open-access and equipped with user-friendly search tool. HealthMap is a database system that collects outbreak data from various sources in both formal and informal. One of the advantages is that HealthMap provide geographical coordinates for the most outbreak cases. The data is not fully accessible in the web site, but the data can be obtained by personal communication to the HealthMap team via email. The WHO DON is an official outbreak notification usually from local or national level public health authorities. Although sensitivity of the system is not higher than other informal data sources listed above, the notified cases are more reliable than the others.

2.2.1.2. Wildlife species richness

International Union for Conservation of Nature (IUCN) (62) has developed comprehensive spatial data of each species' range including terrestrial and marine mammals, and reptiles. The geographical range of avian can be accessible by Birdlife (70) web site. The both data sources were fully open access, with simple process of permission.

2.2.1.3. Socio-demographic factors

Population size (71, 72) and GDP (73) were used in this study to adjust the effect of socio-demographic factors. Both are raster type data created by using national and international agencies' data with a simple interpolation method.

2.2.1.4. Climate

Climate data from WorldClim v2.0 (74) was obtained to adjust its potential confounding effect in the association between species richness and Lassa fever outbreak.

2.2.1.5. Land cover and deforestation

Land cover data were obtained from Tuanmu et al (75) that used four global land cover product; DISCover, GLC2000, MODIS2005, and GlobCover. In terms of forest land cover and deforestation, as a proxy of land cover change, raster data from Global Forest Change (GFC) (76) was incorporated.

2.2.1.6. Geographic factors

Elevation data was obtained from Shuttle Radar Topography Mission (SRTM) data v4.1 (77) which provided 90m scale global elevation data. Although

there have been various altitude data that presented more fine scale, such 30m, the lower resolution map was selected to minimize computational burden. On the other hands, latitude at centroid was extracted directly from the shape file using R v.3.5.0. (78) (the "rgdal" package (79) for shape file importation and the "sp" package for extracting the coordinates (80)).

Table 2-1. Data acquisition

Category1	Category 2	Variables	Data source	Ref
Response variable	Outcome	Lassa fever outbreak	ProMed-Mail Healthmap WHO DON	(1, 65-69, 81, 82)
Main explanatory variables	Wildlife species richness	Rodentia richness	IUCN	(62)
		Carnivore richness	IUCN	
		Accipitridae richness	Birdlife	(70)
		Falconidae richness	Birdlife	
		Strigidae richness	Birdlife	
Covariates	Socio-demography	Population	worldpop	(71, 72)
		GDP	Kummu et al	(73)
	Climate	Precipitation	Worldclim	(74)
		Temperature	Worldclim	
	Forest	Treecover	GFC	(76)
		Treeloss	GFC	
	Land Cover	Cultivated vegetation	Tuanmu et al	(75)
		Urban/Built-up	Tuanmu et al	
	Geography	Elevation	STRM	(77)
		Latitude	-	

2.2.2. Data preprocessing

Data preprocessing has been conducted to create dataset for the analysis from spatial data.

2.2.2.1. Lassa fever outbreak & target study area

The collected Lassa fever outbreak report data from various web-based surveillance system, were organized and assembled with systemic framework. Generally, the framework pursued maximizing sensitivity of search results, so I used search term for ProMED-mail as 'Lassa', and included non-English articles in ProMED-mail (translated by using google translate). On the other hands, the obvious suspected cases, imported cases and human to human cases (usually in the nosocomial environment) were not included. In the post that describe imported cases, I included the localities of the cases' origin if there is evident information to extract them (the final list was illustrated in Appendix 2-1).

2.2.2.2. Wildlife species richness

The species range data of mammals and avian are in the format of polygon. To count the number of species of each class, R function 'intersect' (raster packages (83)) was used. The function enables to calculate the proportion of each species'

ranges intersecting with the given grids. In this study, only species which occupied more than 50% of the given grid considered to count species richness.

In the count of species richness of each order, I excluded species of extinction and possibly extinct. When it comes to carnivores, species in *Panthera* genus (lion, and leopard), and cheetah is not included since they prey mainly on large mammals than rodents (84). Hyena (both spotted hyena and striped hyena) is not included in this study because they are opportunistic scavenger and prey on large mammals (84, 85). Otter species (African clawless otter, camerron clawless otter and spotted-necked otter) were also excluded because its main food source is fish and crab etc. In terms of avian predators, including family *Accipitridae, Falconidae, Strigidae* scavengers (white-backed vultures etc) and species of which prey is mainly aquatic are excluded, in order to focus on the predation pressure towards rodents. (details were described in Appendix 2-2)

2.2.2.3. Socio-demographic factors

As population and GDP data were raster type, I extracted the raster value and summed them for each grid to generate total population size and total GDP in a given grid area. Function 'getValues' was used in package raster (83) and parallel computing has been done with 'foreach' function in package doParallel (86).

2.2.2.4. Climate

The monthly temperature and precipitation data were obtained with raster format. Using 'getValues' function, I averaged the monthly temperature and precipitation in a given grid area. Subsequently, the twelve monthly values of temperature were averaged to generate yearly average and the precipitation values were summed to produce yearly total precipitation.

2.2.2.5. Land cover and deforestation

The twelve land cover data were obtained with raster format and value ranges of each raster cell were between 0 to 100 representing probabilities of the land cover in the raster cells. I used the threshold value as 50 (indicating 50% of probabilities of land use) to categorized the land cover in a given raster cell.

To assess deforestation, I used both forest cover in 2000 and treeloss events from GFC database (76). The forest cover variable was in the format of raster and values ranged from 0 to 100 representing the probabilities of tree canopy presence. As a previous study employed (48), I used 75 as threshold to define forest presence. Subsequently, the treeloss variable, of which format was raster and values are binary, was calculated by product of preprocessed forest present variables and treeloss variables, to count tree loss event only in the presence of forest. These process was followed by a previous study (48).

2.2.2.6. Geographic factors

The elevation variables were provided with raster format, and I used 'getValues' functions to extract and averaging the values in the raster cells to generate average altitude for each grid area.

Table 2-2. Data preprocessing

Category	Variables	Types	Preprocessing
Outcome	Lassa fever outbreak	Polygon	Intersection (50%)
Wildlife species richness	Rodentia	Polygon	Intersection (50%)
	Carnivora	Polygon	Intersection (50%)
	Accipitridae	Polygon	Intersection (50%)
	Falconidae	Polygon	Intersection (50%)
	Strigidae	Polygon	Intersection (50%)
Socio-economic	Population density	Raster	extraction (sum)
	GDP per capita	Raster	extraction (sum)
Climate	Precipitation	Raster	extraction (sum)
	Temperature	Raster	extraction (average)
Landcover	Treecover	Raster	extraction (sum)
	Treeloss	Raster	extraction (sum)
	Cultivated / managed vegetation	Raster	extraction (sum)
	Urban/Built-up	Raster	extraction (sum)
Geography	Elevation	Raster	extraction (average)
	Latitude	Polygon	No needed

2. 2. 3. Statistical analysis

Descriptive analysis was conducted to overview the difference between areas that have experienced Lassa fever outbreak and have not. Mean and standard deviation were provided, and choropleth maps with decile values were also shown to assist understanding of the distributions.

As suggested in the previous section, the variables in this study, specifically, covariates, were included based on the previous finding that both outcome and main explanatory variables were associated, which was not model-based approach. However, not all covariate was included and variable selection process was implemented to avoid a multi-collinearity problem. As previous studies suggested, variables with higher than VIF value 10 (87) and one to one correlation coefficients more than 0.8 were excluded.

Logistic regression models were adopted to examine the associations and both non spatial ordinary model (Generalized linear model, GLM) and spatial model (conditional autoregressive (CAR) model) were employed to consider the potential spatial autocorrelation problem which may exaggerate the association. the models included all selected variables including the three species richness and results were described with odds ratio (OR) and 95% credible interval (95% CI). Goodness of fit was examined by deviance information criterion (DIC) (88). For non-spatial model, Moran's I statistics (89) obtained from testing the residual of the model was also provided. For a Bayesian inference, Bayesian model with Integrated Nested Laplace Approximation (90) was used by the R-INLA package (91).

As a sensitivity analysis, species richness was recounted by including species under the threat of extinction (categorized as VN, EN and CR) and repeated the analysis.

2. 3. Results

2.3.1. Descriptive analysis

The overall descriptive information was shown in Table 2-3. The species richness of rodents was lower in the region with Lassa fever emergence than non-emergence regions (12.82 and 14.73 respectively). Conversely, the species richness of nocturnal predators, and non-nocturnal predators are higher in the region with the emergence (11.29 and 23.91 respectively) than non-emergence regions (11.13 and 21.60 respectively). Population size and GDP were also higher in the emergence regions (146.38 per km^2 and 3668.90 USD per capita) than the others (53.34 per km^2 and 2266.00 USD per capita). In terms of climate, regions with emergence event showed higher annual precipitation (1276.67 mm) than the others (1086.44 mm), but the temperature was higher in non-emergence area (27.18˚C) than the others (26.66 ˚C). Land cover proportions of urban/built-up showed less than 10%. Forest land cover showed higher proportion in the non-emergence regions (7.69% in emergence regions, 10.81% in non-emergence regions), and the difference in cultivated & managed vegetation is relatively large (43.24% in emergence regions, 36.35% in non-emergence regions). Figure 2-3 to 2-13 showed the spatial distribution of the variables.

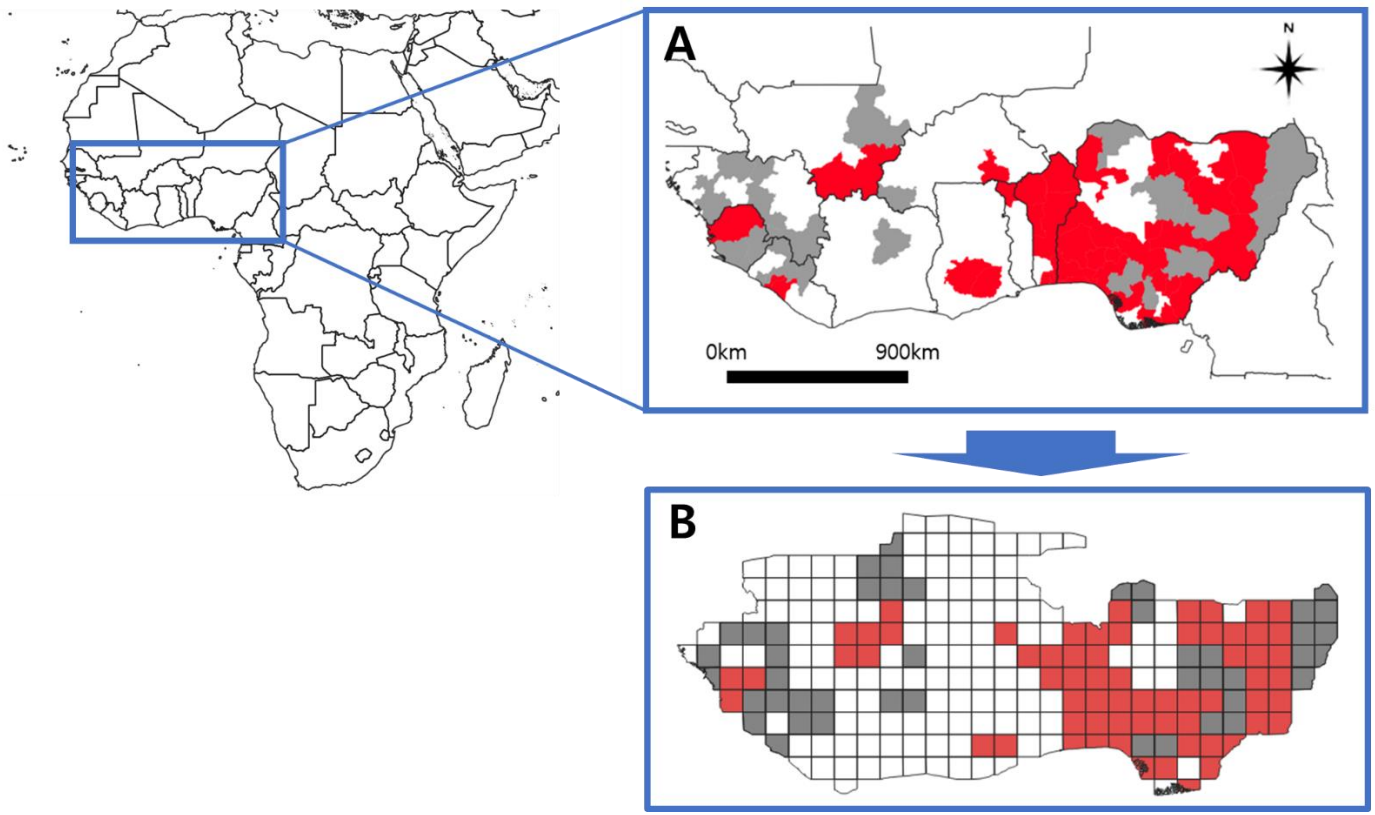

Figure 2-2. Target study area in this study.
Note: Grey area indicated the outbreak reported area before 2005 and red area represent newly reported Lassa fever cases. The white areas indicated the absence of human Lassa-fever cases

Table 2-3. Descriptive analysis

Category1	Category 2	Variables	Mean (±SD)	
			With LF* (N= 65)	Without LF* (N= 126)
Main explanatory variables	Wildlife species richness	Rodents richness	12.82 ± 3.55	14.73 ± 3.65
		Nocturnal predators richness	11.29 ± 2.25	11.13 ± 2.11
		Non-nocturnal predators richness	23.91 ± 2.52	21.60 ± 5.69
Covariate	Socio-economic	Population density (average of 2005, 2010, 2015 per km^2)	146.38 ± 214.74	53.34 ± 82.47
		GDP (USD per capita, 2006 – 2013)	3668.90 ± 1912.21	2266.00 ± 1299.32
	Climate	Precipitation (mm)	1276.67 ± 558.66	1086.44 ± 605.79
		Temperature	26.66 ± 0.83	27.18 ± 1.18
	Forest	Deforestation (2006 -2017, %)	1.67 ± 2.30	1.16 ± 1.56
	Land Cover	Forest (%)	7.69 ± 15.37	10.81 ± 24.01
		Cultivated & managed vegetation (%)	43.24 ± 34.46	36.35 ± 33.19
		Urban/Built-up (%)	0.20 ± 0.78	0.08 ± 0.37
	Geography	Elevation	295.50 ± 153.38	271.98 ± 109.97
		Total space (1000 km^2)	14.16 ± 1.10	14.12 ± 0.98

*LF: Lassa fever

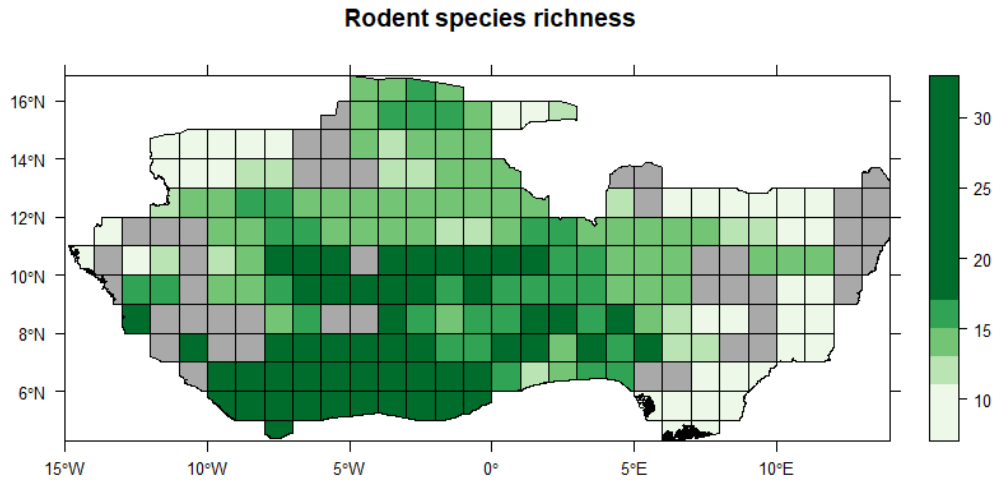

Figure 2-3. Distribution of rodent species richness

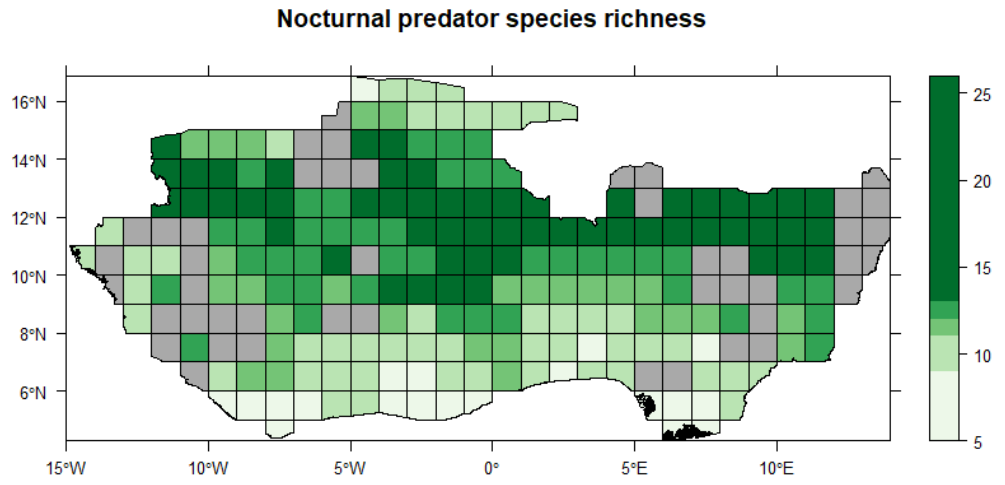

Figure 2-4. Distribution of nocturnal predator species richness

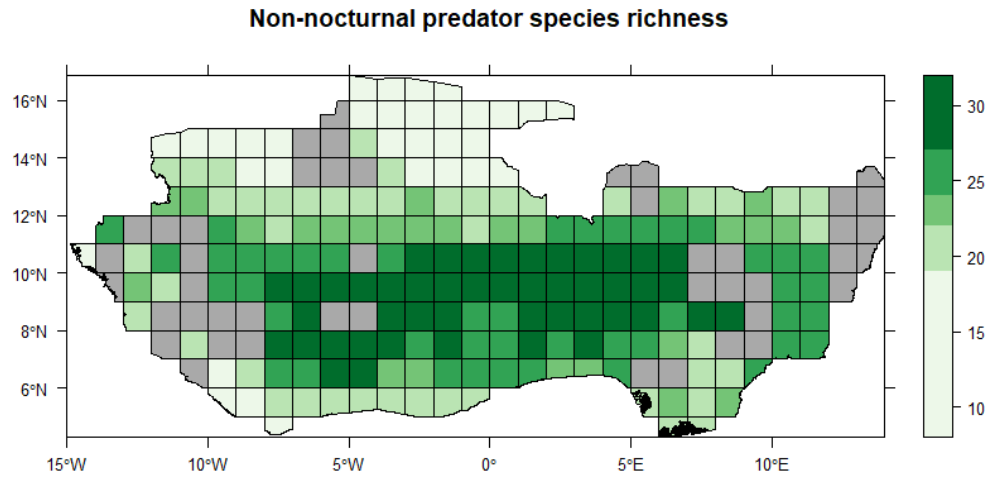

Figure 2-5. Distribution of non-nocturnal predator species richness

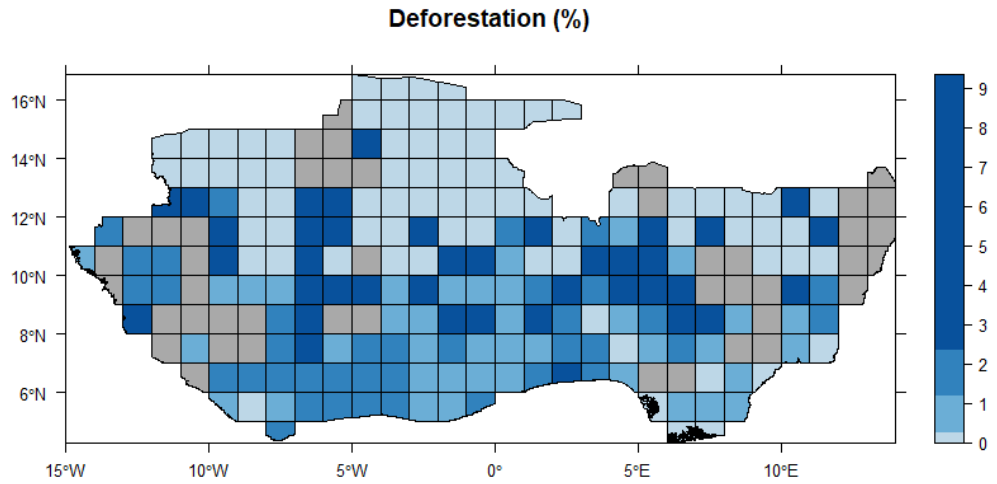

Figure 2-6. Distribution of proportion of deforestation

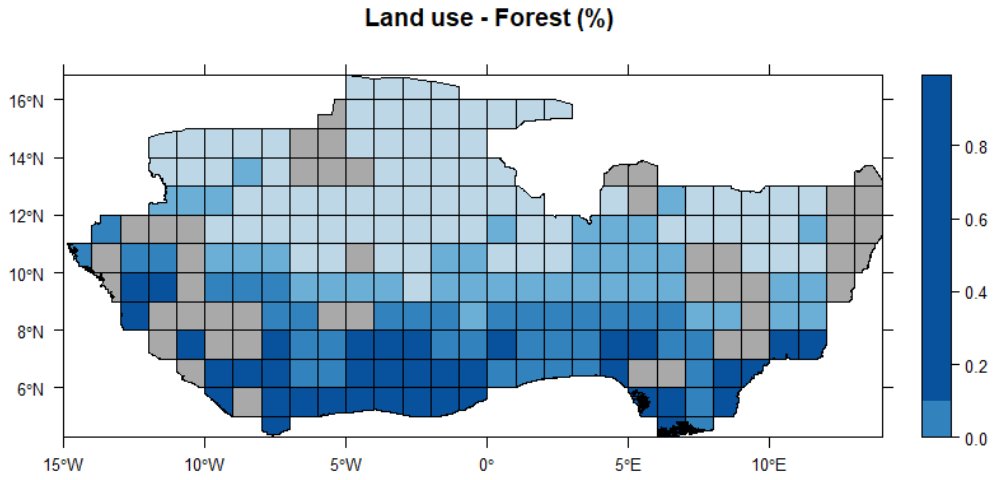

Figure 2-7. Distribution of proportion of forest land cover

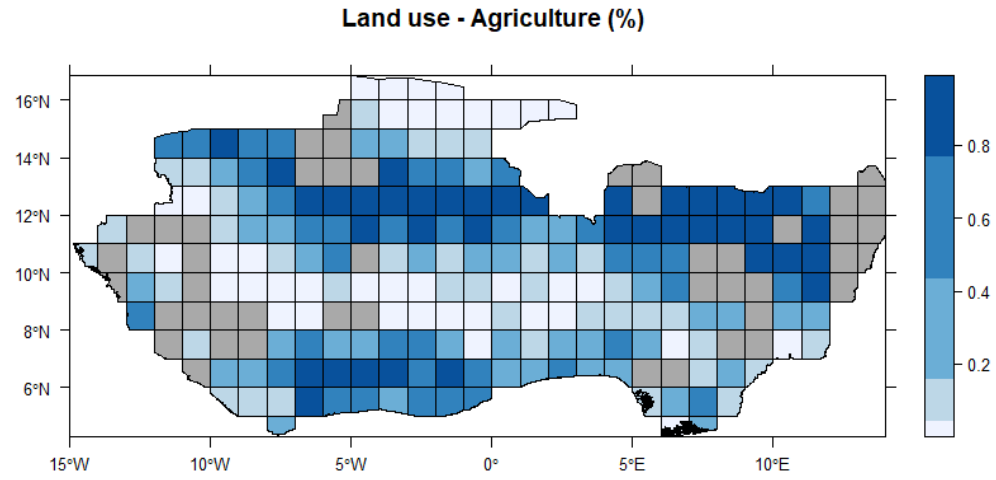

Figure 2-8. Distribution of proportion of agriculture land use

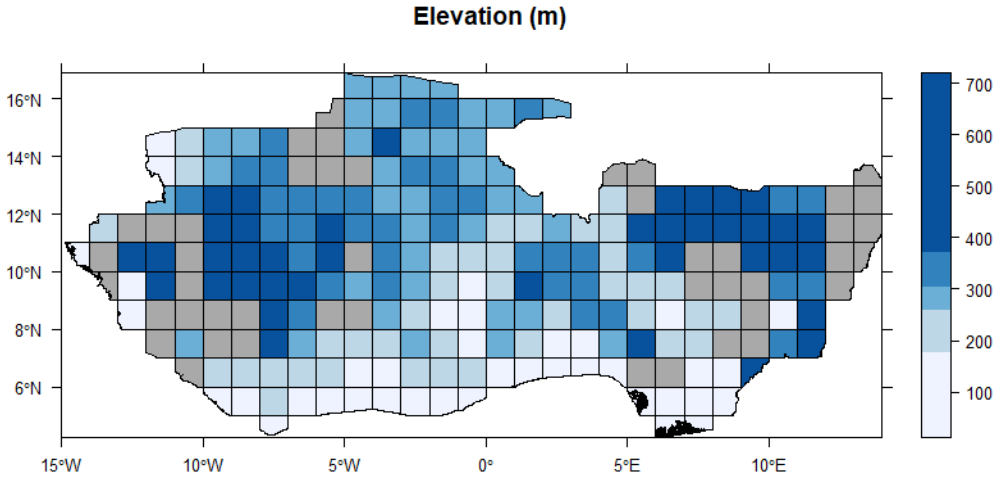

Figure 2-9. Distribution of elevation

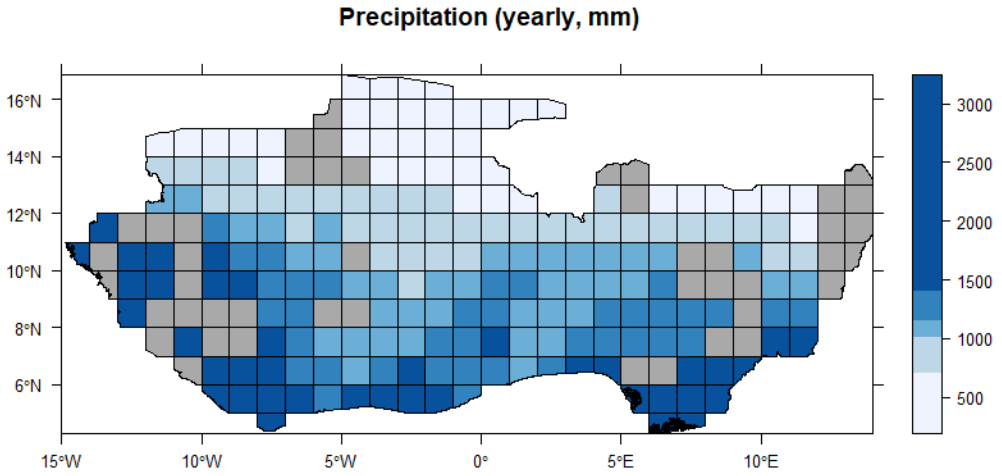

Figure 2-10. Distribution of annual precipitation

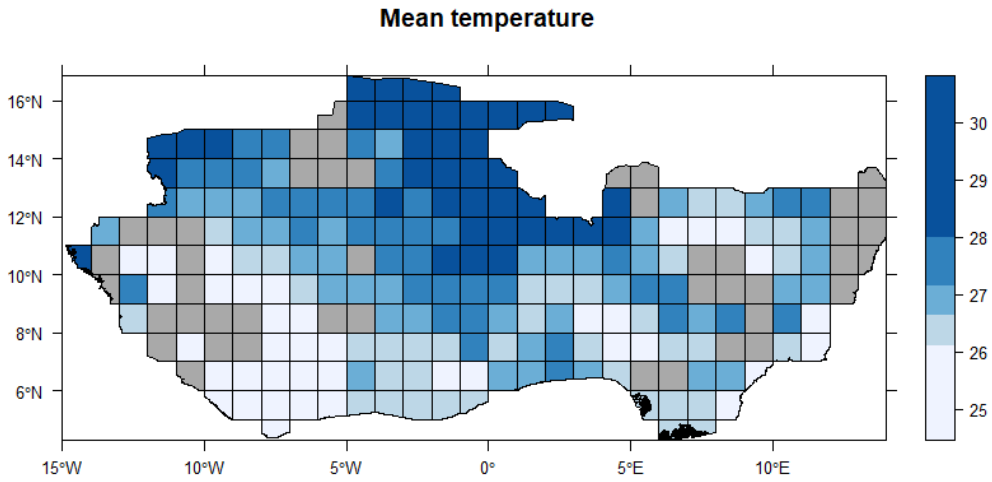

Figure 2-11. Distribution of annual mean temperature

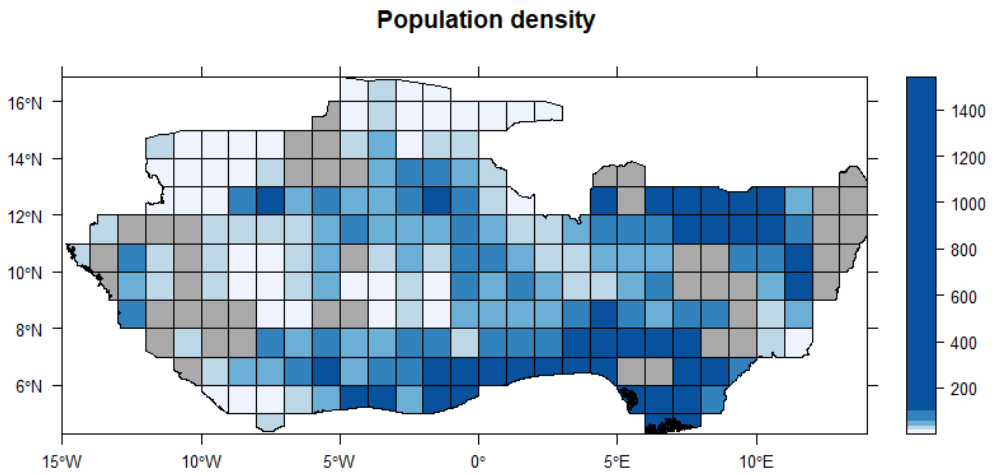

Figure 2-12. Distribution of population density

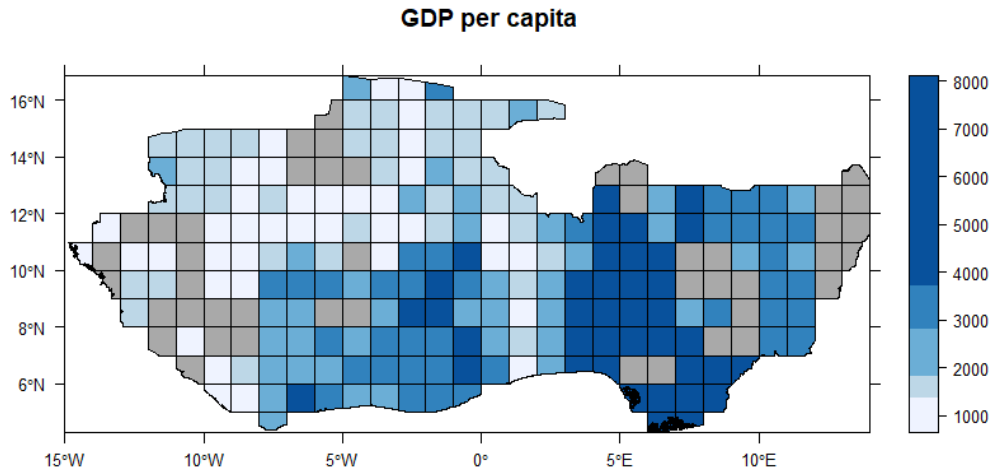

Figure 2-13. Distribution of GDP per capita

2.3.2. Variable selection

In terms of land cover variables, variables were excluded if the proportion of grids which has the land use proportion more than 10%, is less than 10%. As Table 2-4 showed, the proportion of grids that have more than 10% of Urban/Built-up are less than 10% (0 percent), and it was excluded in the analysis.

Table 2-4. Distribution of land cover variables

Land use	Grids of which land use have more than 10%	
	N	%
Forest	38	19.9%
Cultivated vegetation	131	68.6%
Urban/Built-up	0	0.
Total	191	100%

Variable excluded: Urban/Built-up (<10%)

The VIF values were also examined to avoid multi-collinearity problems. As table 2-5 showed, there were no variables that showed VIF value higher than 10 (which is a threshold in this study). Consequently, none of the variables was excluded in the models

Table 2-5. VIF values of the explanatory variables

Category	Variables	VIF
Wildlife species richness	Rodents richness	1.95
	Nocturnal predators richness	3.65
	Non-nocturnal predators richness	2.32
Land use change	Deforestation (2006-2017)	1.12
Land use	Forest	2.92
	Cultivated & managed vegetation	1.86
Geography	Elevation	4.88
	Total land space	1.84
Climate	Precipitation	3.20
	Temperature	5.81
Human-related factors	Population density (per km^2)	2.20
	GDP ($ per capita, 2006 - 2013)	1.68

Note: all variables showed VIF value less than 10, so none of the variables were excluded in the models

One to one correlation was also examined, to prevent the multi-collinearity problems. As Figure 2-14 showed, every combinations of variables had low or moderate correlation, and none of variables was excluded.

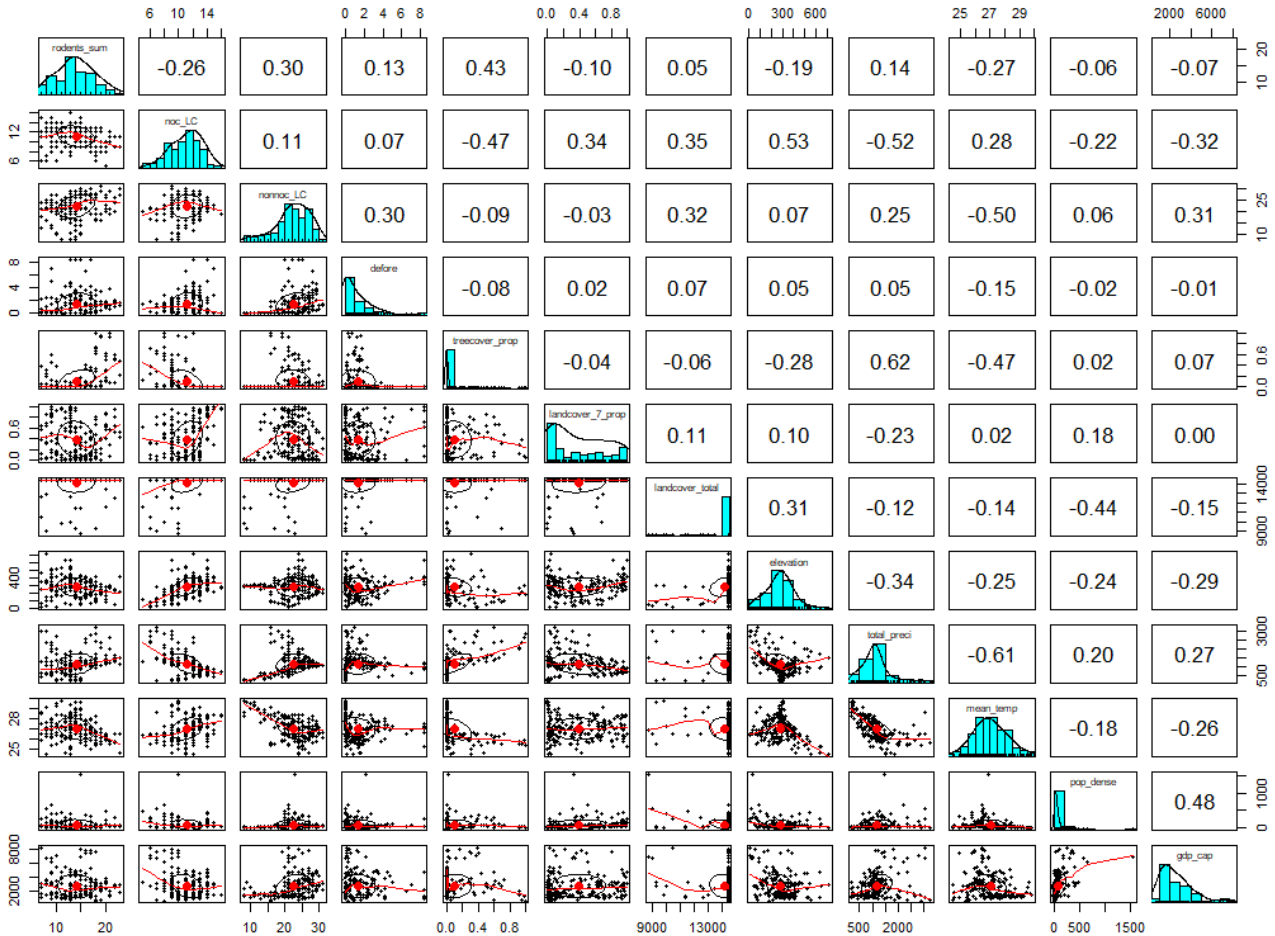

Figure 2-14. One to one correlation of selected variables

2.3.3. Main analysis

Table 2-6 showed main results of this study. The rodent species richness showed significant negative association (OR = 0.835, 95% credible interval (CI) 0.721 – 0.960, for both models), but deforestation (1.224, 1.012 – 1.486 (non-spatial model), 1.224, 1.012 – 1.486 (spatial model)), precipitation (1.001, 1.000 – 1.002 (for both models)), population density (1.009, 1.002 – 1.016 (for both models)), GDP per capita (1.000, 1.000 – 1.001 (for both models)) and total space (1.001, 1.000 – 1.002 (for both models)) showed significant positive association in both non-spatial and spatial models.

Area under curve (AUC) for the GLM model results showed 0.851 indicating that model showed excellent fit for the data. The Moran's I statistics for the residuals of GLM model was 0.093 (p value = 0.015), representing that the level of spatial autocorrelation was low, consequently showed similar results between GLM and CAR models.

Table 2-6. The main results of this study

Variables	Odds ratio (95% CI)	
	GLM	CAR
Rodents	0.835 (0.721 – 0.960)	0.835 (0.721 – 0.960)
Predator (Nocturnal)	1.200 (0.852 – 1.711)	1.200 (0.852 – 1.712)
Predator (Non-nocturnal)	1.111 (0.952 – 1.306)	1.111 (0.952 – 1.306)
Deforestation	1.224 (1.012 – 1.486)	1.224 (1.011 – 1.487)
Land cover – Forest	0.769 (0.020 – 25.170)	0.771 (0.020 – 25.236)
Land cover - Agriculture	1.329 (0.314 – 5.643)	1.330 (0.314 – 5.656)
Elevation	1.002 (0.996 – 1.009)	1.002 (0.996 – 1.009)
Precipitation	1.001 (1.000 – 1.002)	1.001 (1.000 – 1.002)
Temperature	0.988 (0.387 – 2.522)	0.988 (0.387 – 2.523)
Population density	1.009 (1.002 – 1.016)	1.009 (1.002 – 1.016)
GDP per capita	1.000 (1.000 – 1.001)	1.000 (1.000 – 1.001)
Total space	1.001 (1.000 – 1.002)	1.001 (1.000 – 1.002)
DIC	199.67	200.749

Note: The analyses were conducted by logistic regression models and the outcome was whether there have been Lassa fever emergence events (regions with emergence N = 65, without = 126, total N =191). Variables of rodents and predator indicates species richness of each species and species categorized as Least Concern and Near Threatened (by IUCN red list category) were only included to count the species richness.

2.3.4. Sensitivity analysis

Table 2-7 showed main results of this study. The rodent species richness showed significant negative association (0.846, 0.735 – 0.968 (for both models)), but deforestation (1.226, 1.013 – 1.491 (for both models)), precipitation (1.001, 1.000 – 1.002 (for both models)), population density (1.009, 1.002 – 1.016 (for both models)), GDP per capita (1.000, 1.000 – 1.001 (for both models)) and total space (1.001, 1.000 – 1.002 (for both models)) showed significant positive association in both non-spatial and spatial models.

Table 2-7. The results of sensitivity analysis

Variables	Odds ratio (95% CI)	
	GLM	CAR
Rodents	0.846 (0.735 – 0.968)	0.846 (0.735 – 0.968)
Predator (Nocturnal)	1.147 (0.814 – 1.625)	1.147 (0.814 – 1.625)
Predator (Diurnal)	1.075 (0.934 – 1.244)	1.075 (0.934 – 1.244)
Deforestation	1.226 (1.013 – 1.491)	1.226 (1.013 – 1.491)
Land cover – Forest	0.447 (0.011 – 15.291)	0.449 (0.011 – 15.388)
Land cover - Agriculture	1.266 (0.302 – 5.308)	1.268 (0.302 – 5.330)
Elevation	1.003 (0.997 – 1.009)	1.003 (0.997 – 1.009)
Precipitation	1.001 (1.000 – 1.002)	1.001 (1.000 – 1.002)
Temperature	0.982 (0.408 – 2.367)	0.982 (0.407 – 2.369)
Population density	1.009 (1.002 – 1.016)	1.009 (1.002 – 1.016)
GDP per capita	1.000 (1.000 – 1.001)	1.000 (1.000 – 1.001)
Total space	1.001 (1.000 – 1.002)	1.001 (1.000 – 1.002)
DIC	201.17	200.749

Note: The analyses were conducted by logistic regression models and the outcome was whether there have been Lassa fever emergence events (regions with emergence N = 65, without = 126, total N =191). Variables of rodents and predator indicates species richness of each species and species with all red list category were included to count the species richness.

2.4. Discussion

In this chapter, I purposed to examine the association between wildlife species richness and Lassa fever emergence defined as geographic expansion in West Africa region since 2006. Underlying hypothesis was that the higher species richness of rodents and predator may suppress the activities of reservoir rodent population and subsequently reduce the risk of spill-over to human population. The results showed that species richness of rodents had a negatively and statistically significant association with Lassa fever emergence in both non spatial and spatial model, whereas the association with nocturnal and non-nocturnal predators' species richness were not significant in the both non-spatial and spatial models.

In the both main and sensitivity analysis, the associations with rodent species richness were consistent with the previous studies supporting the dilution effect (26). While the dilution effect is more common in nature than amplifying effect for host diversity (43, 45), the dilution effect replicated in this study would be attributed by the high host specificity of Lassa virus. Although there has been other suspected natural host for Lassa virus (*Hylomyscus pamf* and *Mastomys erythroleucus*) (92) other than *M. natalensis*, the other 20 rodent species included in this study area were considered as non-reservoir. This provided suitable conditions that the dilution effect is more likely functioning in that the higher species richness strongly indicated the higher richness of non-reservoir species.

In terms of the effect size, the odds ratio suggested in this study (0.835) would exaggerate relative risk since common outcome was employed in this study

(93). To cope with this issue, modified Poisson regression proposed by Zou (93) was used and produced relative risk as 0.909 (95% CI = 0.850 – 0.972). Considering that inter-quantile range of the rodent species was 5 (minimum = 7, 1st quantile = 12, 3rd quantile = 17, maximum = 23), the risk ratio between 1st quantile regions and 3rd quantile regions was 1.6 (1.15 – 2.25), meaning that 60% higher emergence risk. This implies that the richness of rodent species would be an important predictor for Lassa emergence.

The predator species richness did not show significant associations. While the regulatory effect of predator richness has not been conclusive yet, the study results may also be resulted by dominance status of the reservoirs. As the primary reservoir, *M. natalensis*, is not dominant species in the West Africa (94), and the predation pressure tend to focus on dominant species (95) the effect of predator richness would not be enough to produce noticeable differences.

There are several limitations which should be considered for proper interpretation. First, the study did not consider the changes of species richness in the study period (2006 – 2017). Although the evaluation of spatial distribution and status of extinction threat is regularly updated by IUCN and many experts, it would be impossible to represent the erratic fluctuation and real-time dynamics of species richness change or species extent. But the limitation would be solved in the future studies with better measurements, such as using remote sensing data or internet of things technologies. Second, the other species which is not incorporated in this study may affect the association. For example, there are several species in insectivore which

are in the same trophic hierarchy as rodents could limit the rodent population as competitors. Third, as the population size data for each species was not possible to obtain, the effect of evenness of wildlife cannot be examined but it would influence the disease transmission dynamics as well. Although it would be impractical to obtain global level population trend of each species, a systematic local-level survey would be possible and needed for ecological study and also public health purpose. Fourth, the study unit, that one-degree grid was used in this study, would affect the results, in that different scale of study unit (e.g, point five-degree grid) would produce different sample size and values in explanatory variables (Modifiable area unit problem, MAUP).

Nevertheless, the study results had important implication on both public health and wildlife conservation. In the human public health perspectives, the founded association could be applied to predict the risk areas considering the fluctuation of species richness. Moreover, because the increasing predator species richness could be a practical intervention (there is already an activated project), fundamental and pre-emptive countermeasures with ecological point of view would be developed with collaboration with environmental department.

Chapter III.

The effect of wildlife biodiversity on Hantavirosis incidence in Brazil

3.1. Introduction

3.1.1. Impact of hanta virus in Brazil

Hantavirosis is the one of the globally distributed rodent-borne diseases (RBDs), transmitted by urines or feces of natural reservoir, and annual incidence would be approximately 150,000 cases worldwide (96). Various types of virus have been discovered such as Hantaan virus (China, South Korea), Seoul virus (worldwide), Sin Nombre virus (North Americas) etc., and these can be categorized by geographical range; New world hantavirus which is related to hantavirus pulmonary syndrome (HPS) and old world hantavirus which occur hemorrhagic fever with renal syndrome (HFRS) (96).

In Brazil, HPS is the main concern, of which clinical presentations include fever, dyspnea, myalgia, cough tachycardia etc., and case-fatality is between 33% to 100%, varied depends on the regions (97). The number of cases has increased recently. The total cumulative number of cases until 2001 was 134, but it surged to 1,252 cases until 2009 (97, 98).

3.1.2. Previous studies on hantavirus in Brazil

To cope with the emerging threat, a number of studies have been conducted to find risk factors of the hantavirosis. Majority of studies pointed out that deforestation (or fragmentation of forest) (99) and anthropogenic changes on landuse could increase the risk of hantavirosis (13), by increasing the chance of contact

between reservoir species and human. The resilience of reservoir rodents, which can be survived and even thrive in anthropogenic defaunation environment as a generalist species (100), also contribute the association between deforestation and the disease incidence.

Climate and meteorological factors could also affect the disease dynamics by changes in virus survival environment and habitat niche of rodents (13). Recent climate change has also been considered as drivers, and Prist et al found that temperature anomalies alone could increase the risk from 1.6% to 1.7% (14).

Socio-economic status could influence the disease outbreak. Agricultural practice, such as sugarcane production in Brazil (14), and economic conditions could affect the incidence (12) by linking to public awareness and practice on minimizing human-host contact

The role of wildlife diversity has also been studied. For example, some studies suggested that host (natural host, in this case rodent reservoir) diversity may decrease the risk of spillover by reducing contact rate between natural hosts, followed by decreased diseases prevalence in the natural host population (45). The theory was called 'Dilution effect', and many field experiments, observational studies (26, 43) and theoretical modelling studies (46, 101) have supported the effect but the arguments are still ongoing and the conclusion has not reach a consensus (25).

On the other hand, the effect of predators has been relatively neglected (42). Although the plausibility of predators' regulation effect has been discussed and has

long history (34), supporting evidence has been lacked, and only recently reported in tick-borne disease (39) or hantavirosis (38), but direct link between human spillover and predator related factors were not well-studied.

3.1.3. The goal of study and study design

In this chapter, the association of wildlife diversity with hantavirosis incidence was investigated to examine dilution effect and also the effect of predators' diversity including both mammals (*Carnivore*) and avian species (*Accipitridae*, *Falconidae* and *Strigidae*).

In terms of species richness, three variables were employed as the major explanatory factors; rodent species richness, diurnal predator species richness and non-diurnal predator species richness. The rodent species richness was incorporated to investigate whether the dilution effect works for preventing hantavirosis incidence in Brazil, and the predator species richness was included to examine the suppression effect of predators on the spill-over event.

De Oliveira et al (102) reported 8 potential reservoir rodents species; *Oligoryzomys nigripes, Oligoryzomys fornesi, Oligoryzomys utiaritensis, Oligoryzomys microtis, Necromys lasiurus, Holochilus sciureus, Akodon montensis, Calomys callidus*. Most of them were reported as nocturnal species (103) except *Necromys lasiurus* which showed higher activity in the daytime (104). Supposing that the effect size of diurnal predators' regulation on the diurnal reservoir and that of

nocturnal predators on the nocturnal reservoirs would be different, the effects of diurnal and nocturnal predators were discretely tested. In addition, species which were under threat of extinction were not included in the main analysis, because species with relatively lower population would not be influential enough. To this end, species categorized as “Least Concern (LC)” or “Near threatened (NT)” by IUCN (62) were included and the others (“Vulnerable (VN)”, “Endangered (EN)”, “Critically Endangered (CR)”) were excluded in this study.

3.2. Materials and methods

3.2.1. Data acquisition

To examine the study hypothesis, various types of data representing Hantavirosis outbreak (main outcome), species richness of wildlife (main explanatory variables), and other covariates, including anthropogenic, climate, land cover, and geographic factors, were needed. Although there was no systematic data collection that covered all of these variables from single source of database, the feature of spatial data that can be merged based on common spatial attributes, enables to comprehensively utilize a number of data from various sources (Table 3-1).

3.2.1.1. Hantavirosis incidence

The number of hantavirosis cases was obtained from SINAN database (105, 106). The cases number can be downloaded by geographical categories, and available period was between 2007 and 2014. Since it was in the format of excel file, no preprocessing was required.

3.2.1.2. Wildlife species richness

International Union for Conservation of Nature (IUCN) has developed comprehensive spatial data of mammal species. The data is fully open access and conveniently downloadable with shape format. The data has distribution range

information of 5,303 mammal species worldwide with polygon format. The shape file also includes IUCN categories and criteria that intuitively indicate current status of each species for extinction.

The spatial data was originated from the maps collected by Sechrest in 2003 (107) which illustrated geographical ranges of some species, and later, expert editing has been conducted to improve quantities and qualities (108).

3.2.1.3. Socio-demographic and economic factors

Population size and regional GDP by municipality were used in this study to adjust the effect of anthropogenic factors. IBGE (109-111)

3.2.1.4. Climate

Climate data from WorldClim (74) was used to adjust its potential confounding effect in the association between species richness and Lassa fever outbreak.

3.2.1.5. Land cover and deforestation

Land cover data were obtained from Tuanmu et al (75) that used four global land cover product; DISCover, GLC2000, MODIS2005, and GlobCover. As a proxy of

land cover change, deforestation data from Global Forest Change (GFC) (76) was incorporated.

3.2.1.6. Geographic factors

Elevation data was obtained from David et al (112) which provided 1km scale global elevation data. Although there have been various altitude data that presented more fine scale, such 30m, the lower resolution map was selected to minimize computational burden. On the other hands, latitude at centroid was extracted directly from the shape file using R v.3.5.0 (78) (rgdal package (79), sp package (80)).

Table 3-1. Data acquisition

Category1	Category 2	Variables	Data source	Ref
Response variable	Outcome	Hantavirosis incidence	SINAN	(113)
Main explanatory variables	Diversity	Rodentia	IUCN	(62)
		Carnivora	IUCN	
		Accipitridae	Birdlife	(70)
		Falconidae	Birdlife	
		Strigidae	Birdlife	
Covariate	Deforest	Treeloss	GFC	(76)
	Demography	Population	DATASUS	(114)
		% of urban population	IBGE	(110)
	Economy	GDP	IBGE	(109)
	Climate	Temperature	Worldclim	(74)
		Precipitation	Worldclim	
	Meteorology	Land surface temperature	NASA MODIS	
	Landuse	Forest	GFC	(76)
		Cultivated vegetation	Earthenv	(75)
		Urban/Built-up	Earthenv	
	Crop produnction	Corn	IBGE	(111)
		Soya	IBGE	
		Sugarcane	IBGE	
	Geography	Elevation	STRM	(77)
		Latitude	-	

3.2.2. Data preprocessing

Data preprocessing has been conducted to create dataset for the analysis from spatial data.

3.2.2.1. Brazil administrative unit adjustment

The obtained brazil map with administrative border (municipality levels) from GADM (115) showed 5,564 municipalities in Brazil, but some data from IBGE, such as population and regional GDP has information of 5,570 municipalities. This is because the number has been increased from 2009. Considering that study period was between 2007 to 2014, the different administrative classification between years was standardized as 5,564. (details were illustrated in Appendix 3-1)

3.2.2.2. Wildlife species richness

The species range data of mammals and avian are in the format of polygon. To count the number of species of each class, R function 'gIntersection' was used. The function enables to digitalize whether the ranges of each species intersect the given grid or not. By summing the species intersection by their categories in a given grid, the species richness was obtained.

In the count of species richness of each order, I excluded species of extinction and possibly extinct. When it comes to carnivores, species in *Panthera*

genus (lion, and leopard), and cheetah is not included since they prey mainly on large mammals than rodents (Details are described in Appendix 3-2)

3.2.2.3. Anthropogenic factors

Since GDP data between 2011 and 2014 were not provided in IBGE, GDP values in 2010 was used for imputation, supposing that the differences between municipalities were not considerably different between 2011 and 2014. No more preprocessing was required as it was provided by table format.

3.2.2.4. Climate

The monthly temperature and precipitation data were obtained with raster format. Using 'getValues' function, I averaged the monthly temperature and precipitation in a given municipality polygon and then averaged the twelve monthly values to generate yearly average.

3.2.2.5. Land cover and deforestation

The twelve land cover data were obtained with raster format and value ranges of each raster cell were between 0 to 100 representing probabilities of the land cover in the raster cells. I used the threshold value as 50 (50%) to classify the land cover in a given raster cell.

To assess deforestation, I used both forest cover in 2000 and treeloss events from GFC database (76) The forest cover variable was in the format of raster and values ranged from 0 to 100 representing the probabilities of tree canopy presence. As a previous study employed (48) I used 50 as threshold to define forest presence. Subsequently, the treeloss variable, of which format was raster and values are binary, was calculated by product of preprocessed forest present variables and treeloss variables, to count tree loss event only in the presence of forest. These process was followed by a previous study (48)

3.2.2.6. Geographic factors

The elevation variables were provided with raster format, and I used 'getValues' functions to extract and averaging the values in the raster cells to generate data for each municipality polygon.

Table 3-2. Data preprocessing

Category	Variables	Data type	preprocessing
Outcome	Hantavirosis incidence	Table	No needed
Diversity	Rodentia	Polygon	Intersection
	Carnivora	Polygon	Intersection
	Raptor	Polygon	Intersection
	Strigidae	Polygon	Intersection
Socio-economic status	Population	Table	No needed
	% of urban population	Table	No needed
	GDP	Table	No needed
Climate	Temperature	Raster	Extraction
	Precipitation	Raster	Extraction
Land cover & Land cover change	Forest	Raster	Extraction
	Cultivated vegetation	Raster	Extraction
	Urban/Built-up	Raster	Extraction
	Deforestation	Raster	Extraction
Crop production	Corn	Table	No needed
	Soya	Table	No needed
	Sugarcane	Table	No needed
Geography	Elevation	Raster	Extraction
	Latitude	Table	No needed

3.2.3. Statistical analysis

Descriptive analysis was conducted to overview the difference between areas that have experienced Hantavirosis outbreak between 2007 and 2014 and have not. Mean and standard deviation were provided, and choropleth maps with decile values were also shown to assist understanding of distributions.

As suggested in the previous section, the variables in this study, specifically, covariates, were included based on the previous finding that both outcome and main explanatory variables were affected, which is not model-based approach. However, not all covariate was included and variable selection process was implemented to avoid multi-collinearity issue. As previous studies suggested, variables with higher than VIF value 10 (87) and one to one correlation coefficients more than 0.8 were excluded.

Logistic regression models were adopted to examine the associations and Bayesian models with Integrated Nested Laplace Approximation (90) were employed by using the R-INLA package (91) for a Bayesian inference. Considering the potential spatial autocorrelation problem which may exaggerate the associations, Moran's I statistics (89) were estimated for the residuals of non-spatial GLM, and CAR models were employed if spatial autocorrelation were detected. The models included all selected variables including the three species richness and results were described with odds ratio (OR) and 95% credible interval (95% CI). Goodness of fit was examined by deviance information criterion (DIC) (88).

As a sensitivity analysis, species richness was recounted by including species under the threat of extinction (categorized as VN, EN and CR) and repeated the analysis.

3. 3. Results

3.3.1. Descriptive analysis

The overall descriptive information was presented in Table 3-3. The species richness of rodents, diurnal predators, and non-diurnal predators are higher in the regions with hantavirosis incidence (as 28.5, 36.0 and 16.7 respectively) than non-incidence regions (the species richness was 26.9, 34.5 and 12.9 respectively). Population density and percent of urban population was also higher in the incidence-experienced regions (156.3 and 73.7 percent, respectively) than the others (108.0 and 63.2 percent, respectively). In terms of climate, regions with hantavirosis event showed higher annual precipitation level (1618.1 mm) than the others (1363.6 mm), but the temperature was higher in non-incidence municipalities (22.4 ^{0}C) than the others (20.1 ^{0}C).

Land cover proportions of urban/built-up showed less than 10%. Forest cover was higher in the regions with hantavirosis incidence (39.0% in incidence regions, 29.7% in non-incidence regions), but deforestation proportion was higher in the regions without hantavirosis (5.9% in non-incidence regions, 5.0% in incidence regions). Cultivated & managed vegetation is relatively higher in non-outbreak regions (46.3% in non-incidence regions, 42.8% in incidence regions)

Table 3-3. Descriptive analysis

Category 1	Category 2	Variables	Mean (±SD)	
			With Hantavirosis (N = 346)	Without Hantavirosis (N = 5,217)
Main exposure	Diversity	Rodents species richness	28.51 ± 5.2	26.90 ± 7.4
		Diurnal predators species richness	35.96 ± 3.7	34.54 ± 4.7
		Non-diurnal predators species richness	16.71 ± 2.6	12.88 ± 4.4
Covariate	Socio-economic status	Population density (km^2)	156.29 ± 631.0	108.04 ± 586.8
		Urban population (%)	73.72 ± 23.1	63.17 ± 21.8
		Regional GDP per capita (USD 10^3)	19.51 ± 17.3	11.30 ± 12.8
	Climate	Annual mean temperature (1970 – 2000, ˚C)	20.13 ± 2.9	22.38 ± 2.9
		Annual total precipitation (1970 – 2000, mm)	1618.14 ± 247.7	1363.60 ± 427.5
	Land use & Land cover change	Forest (%)	38.98 ± 28.0	29.74 ± 24.5
		Cultivated and managed vegetation (%)	42.77 ± 30.8	46.27 ± 31.4
		Urban/Built-up (%)	1.29 ± 6.6	0.54 ± 4.7
		Deforestation (% between 2007 - 2014)	4.99 ± 4.6	5.93 ± 6.0
	Crop production	Corn (10^3 tons)	37.3 ± 114.7	9.63 ± 34.5
		Soya (10^3 tons)	41.19 ± 164.3	10.57 ± 45.7
		Sugarcane (10^3 tons)	343.77 ± 896.3	112.47 ± 373.6
	Geography	Elevation (m)	463.43 ± 268.6	329.25 ± 253.5
		Latitude	-22.11 ± 6.1	-16.08 ± 8.3
		Total space (km^2)	2683.98 ± 11419.9	1451.74 ± 5000.0

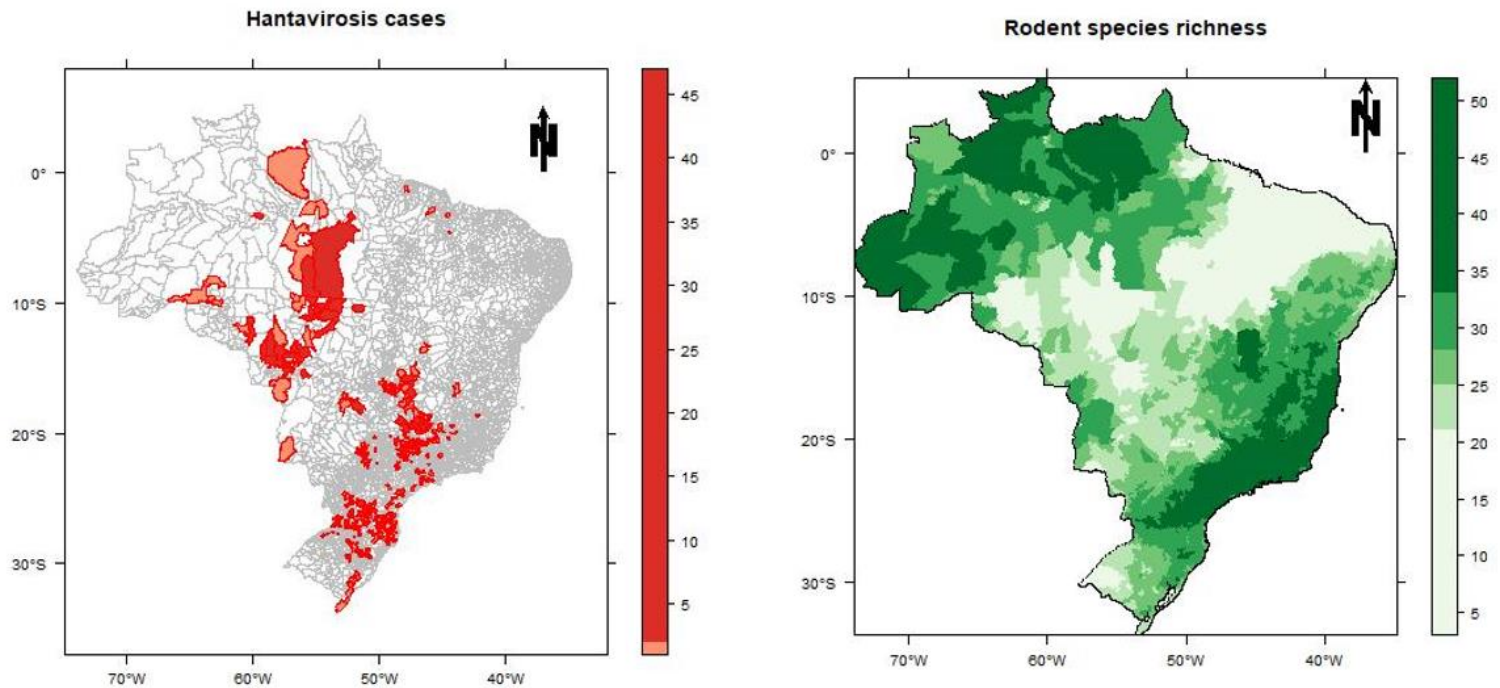

Figure 3-1. Distribution of hantavirosis incidence cases between 2007 and 2014 (left) and rodent species richness (right)

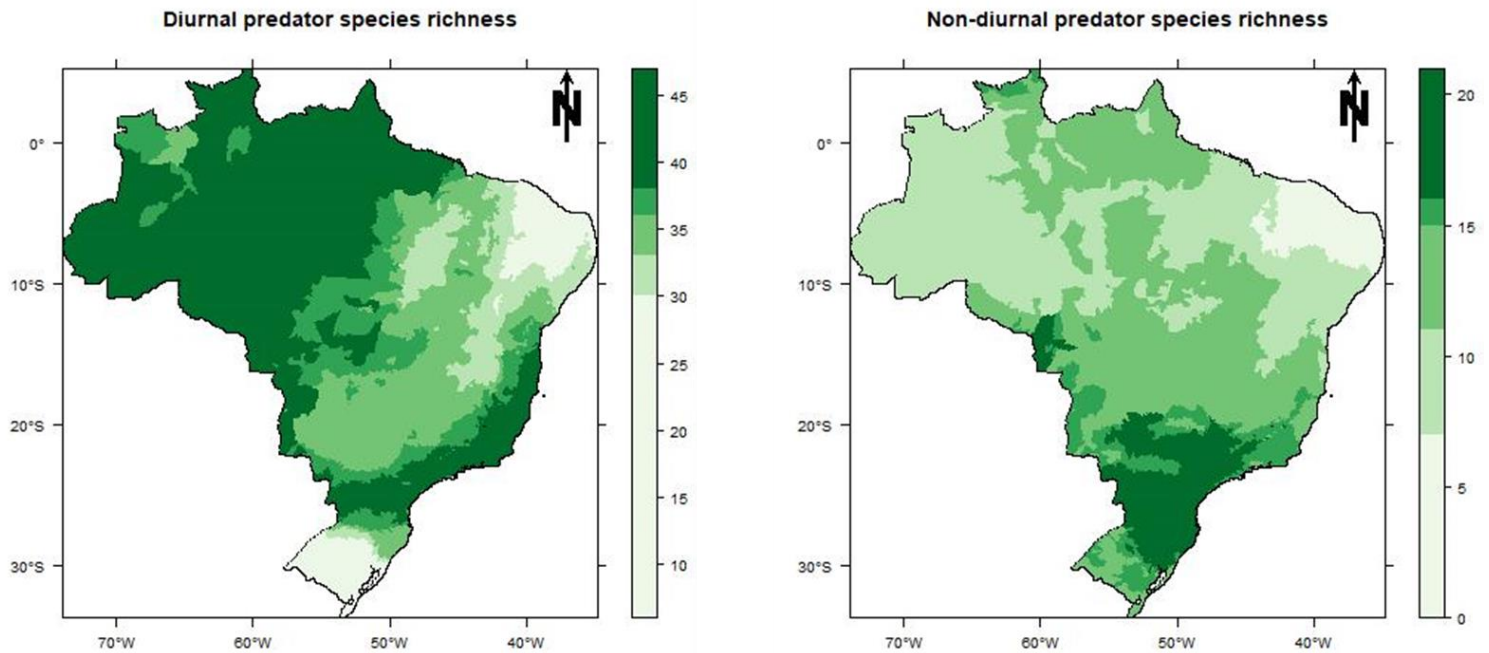

Figure 3-2. Distribution of diurnal species richness (left) and non-diurnal species richness (right)

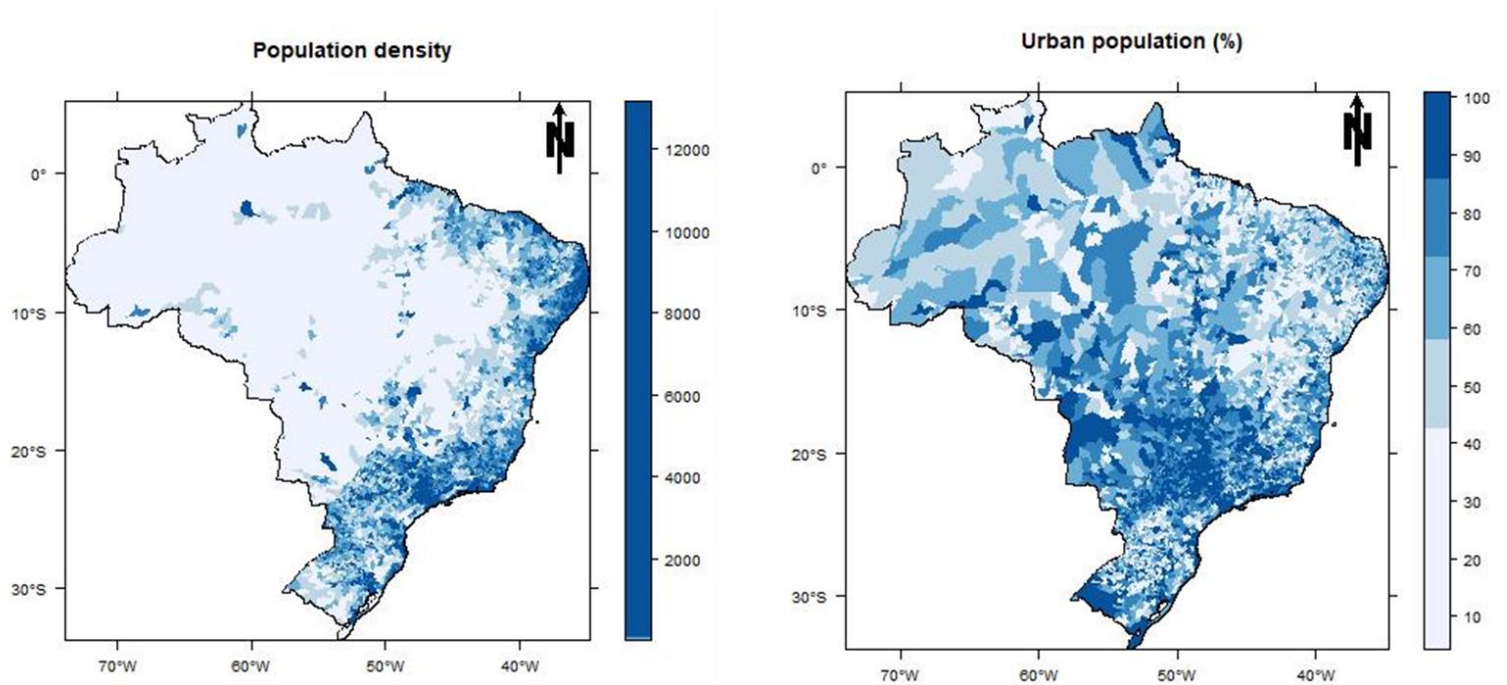

Figure 3-3. Distribution of population density (left) and urban population (right)

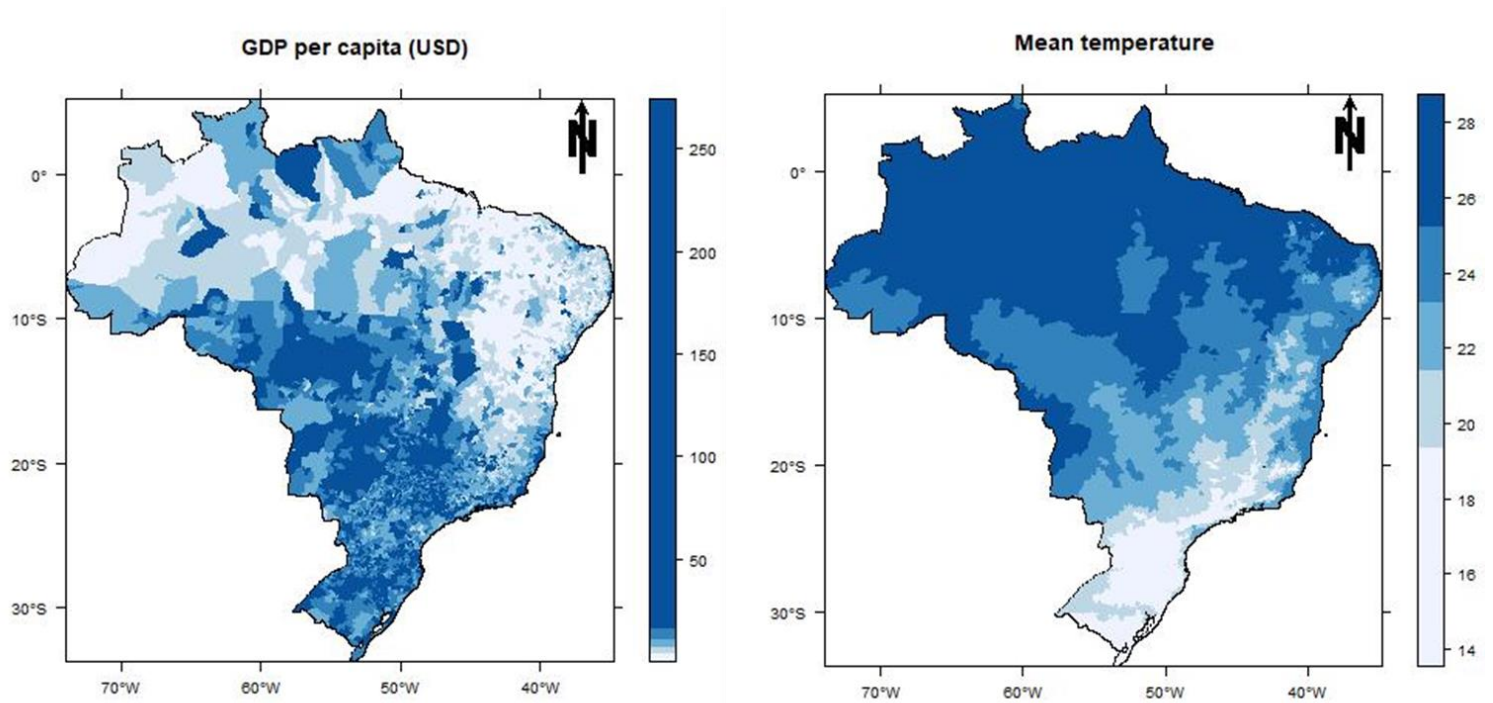

Figure 3-4. Distribution of GDP per capita (left) and annual mean temperature (right)

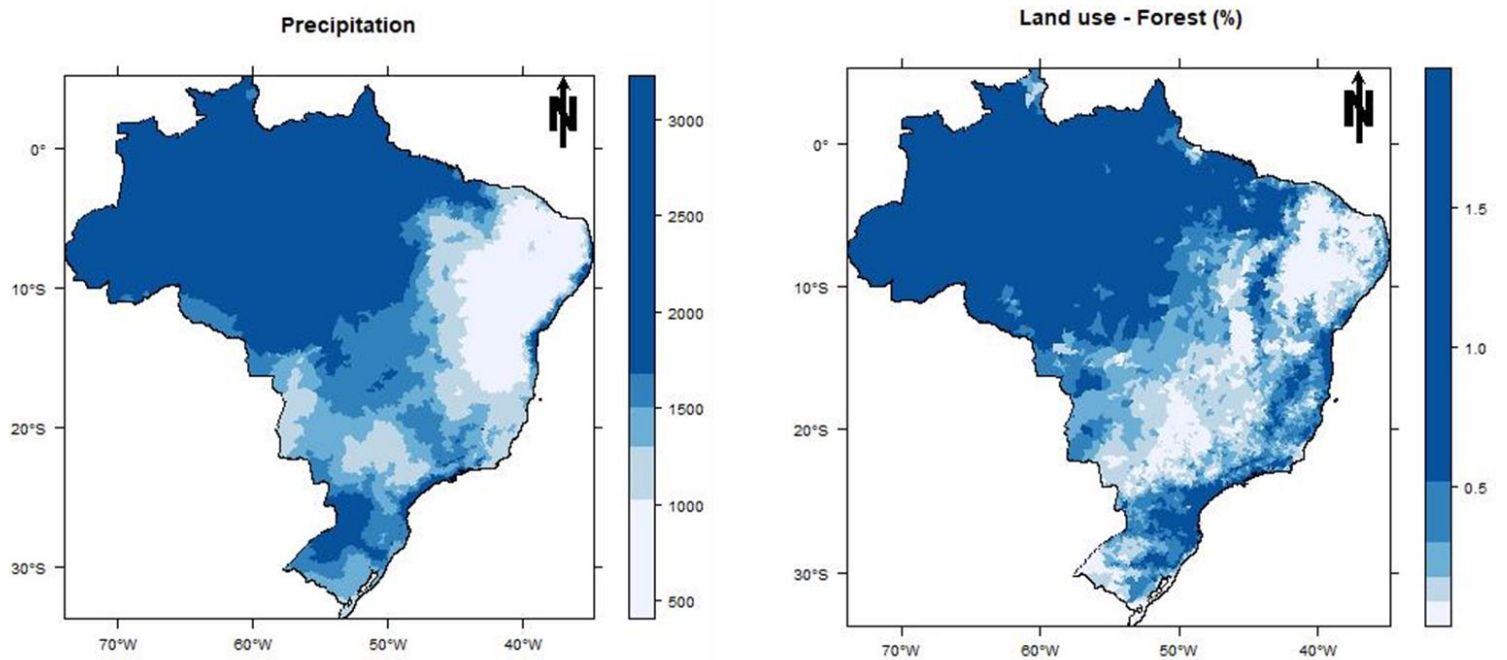

Figure 3-5. Distribution of annual total precipitation (left) and forest land cover (right)

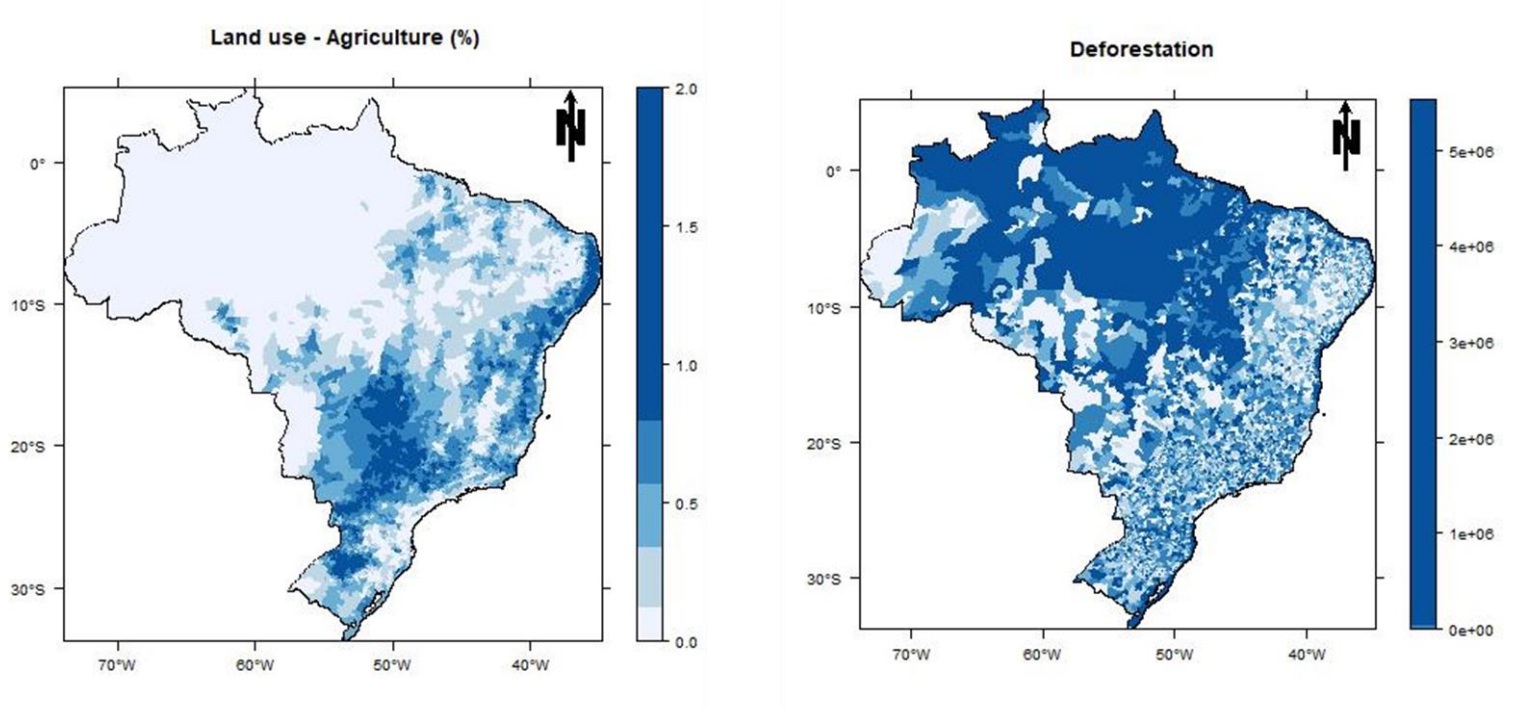

Figure 3-6. Distribution of agricultural land use (left) and deforestation (right)

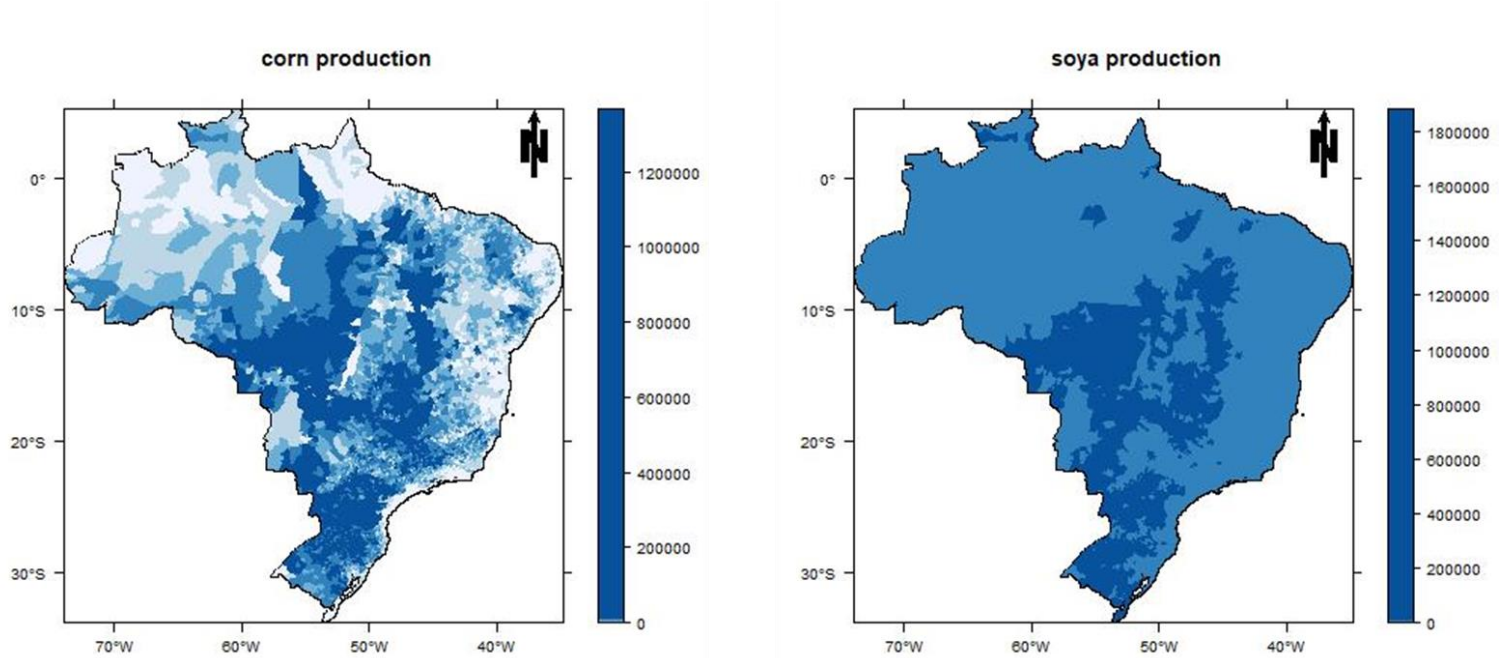

Figure 3-7. Distribution of corn production (left) and soya production (right)

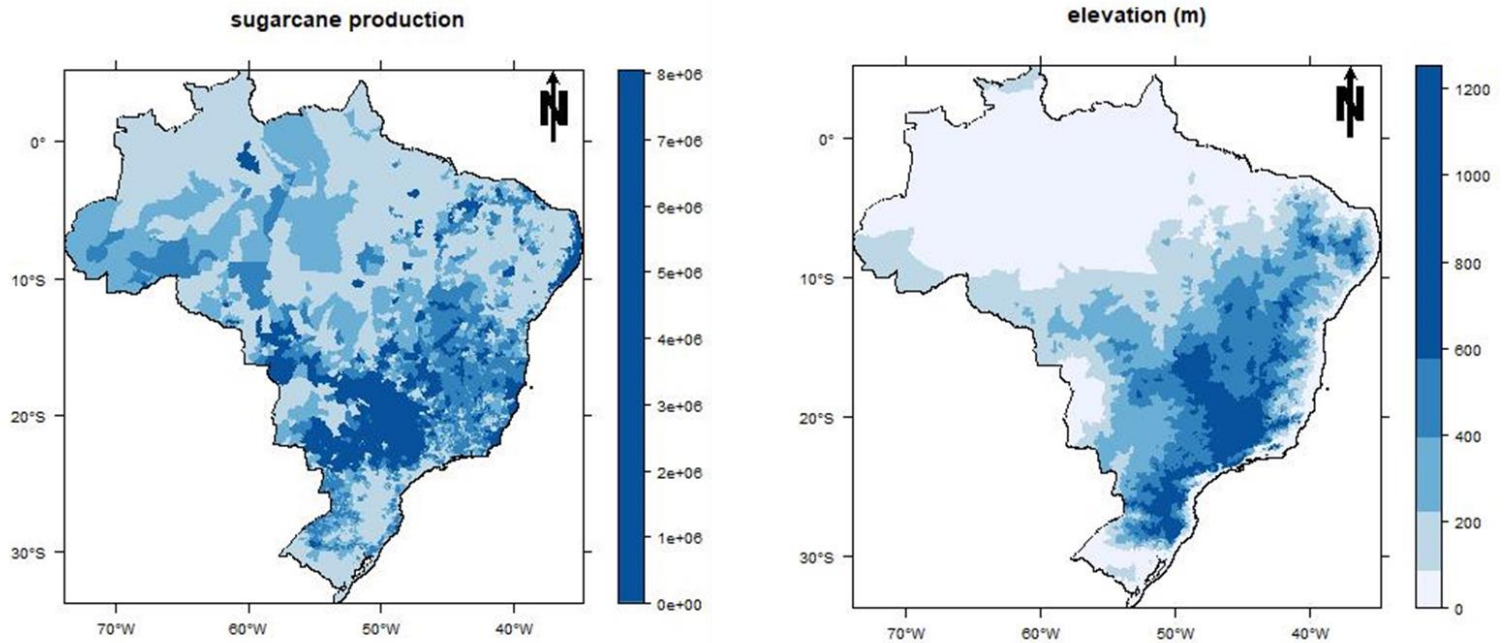

Figure 3-8. Distribution of sugarcane production (left) and elevation (right)

Table 3-4. The potential contribution of each reservoir on hantavirosis

Species	Behaviour	Number of cases (total 861 cases)	Number of Municipalities (total 5,563)
Oligoryzomys nigripes	Nocturnal	642	3981
Necromys lasiurus	Diurnal	702	4859
Calomys callosus	Nocturnal	161	1492
Holochilus sciureus	Nocturnal	341	2180
Oligoryzomys microtis	Nocturnal	149	199
Akodon montensis	Nocturnal	423	2238
Oligoryzomys fornesi	Nocturnal	167	1565

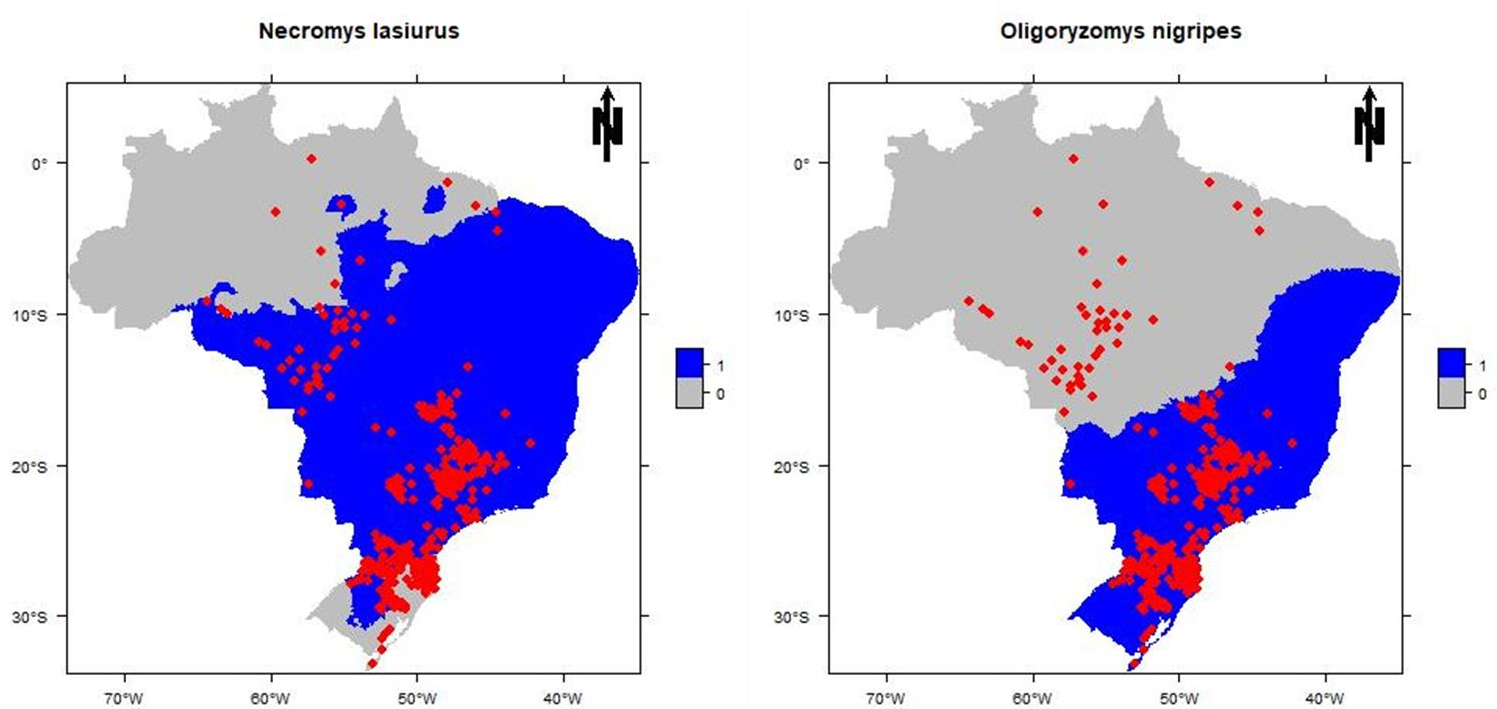

Figure 3-9. Distribution of reservoir rodent species; *Necromys lasiurus* (left) and *Oligoryzomys nigripes* (right)

Note: the blue describe the presence of the rodent species and red dots indicate municipalities with hantavirus report

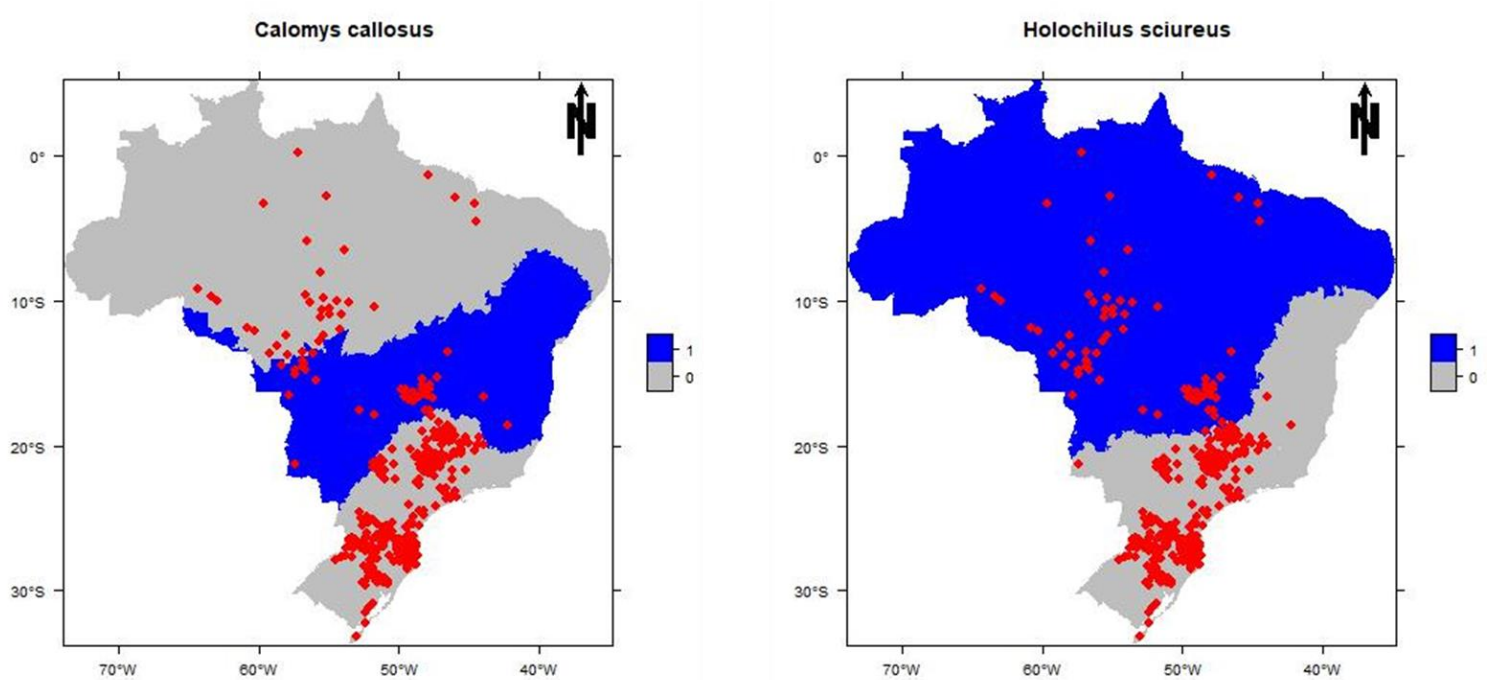

Figure 3-10. Distribution of reservoir rodent species; *Calomys callosus* (left) and *Holochilus sclureus* (right)

Note: the blue describe the presence of the rodent species and red dots indicate municipalities with hantavirus report

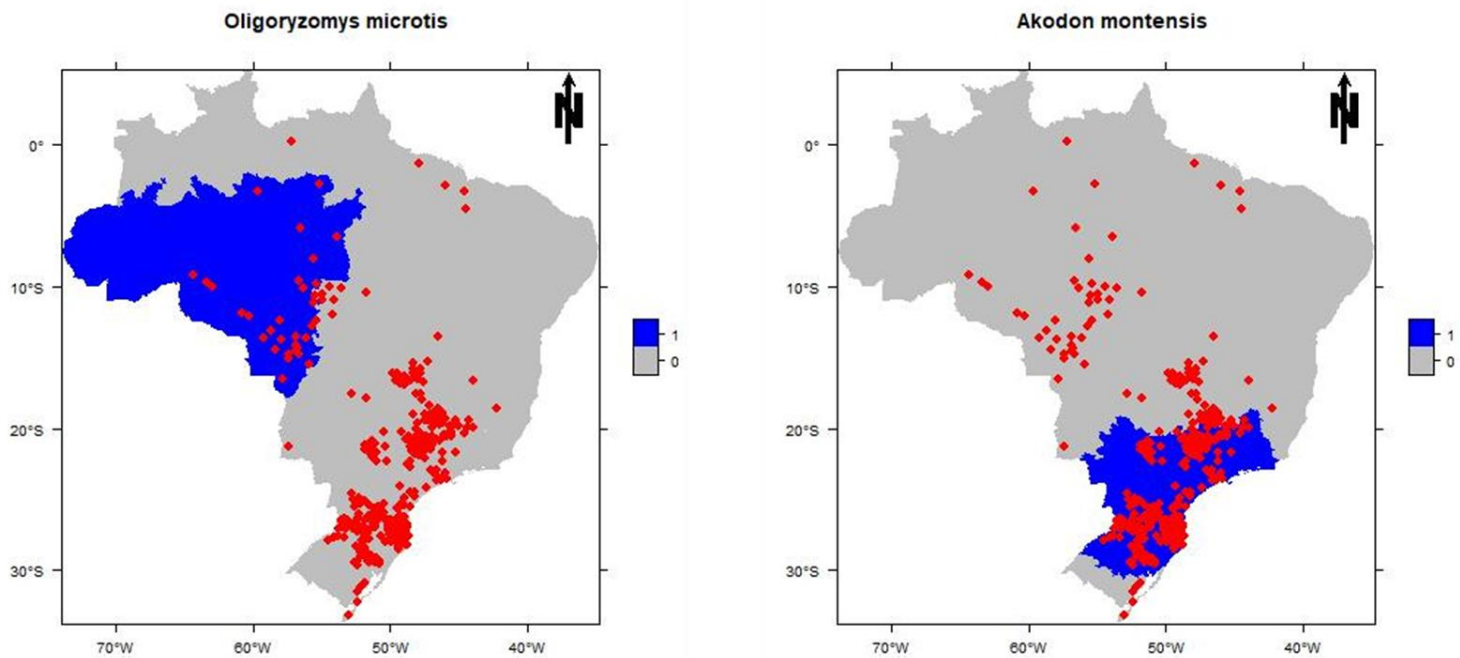

Figure 3-11. Distribution of reservoir rodent species; *Oligoryzomys microtis* (left) and *Akodon montensis* (right)

Note: the blue describe the presence of the rodent species and red dots indicate municipalities with hantavirus report

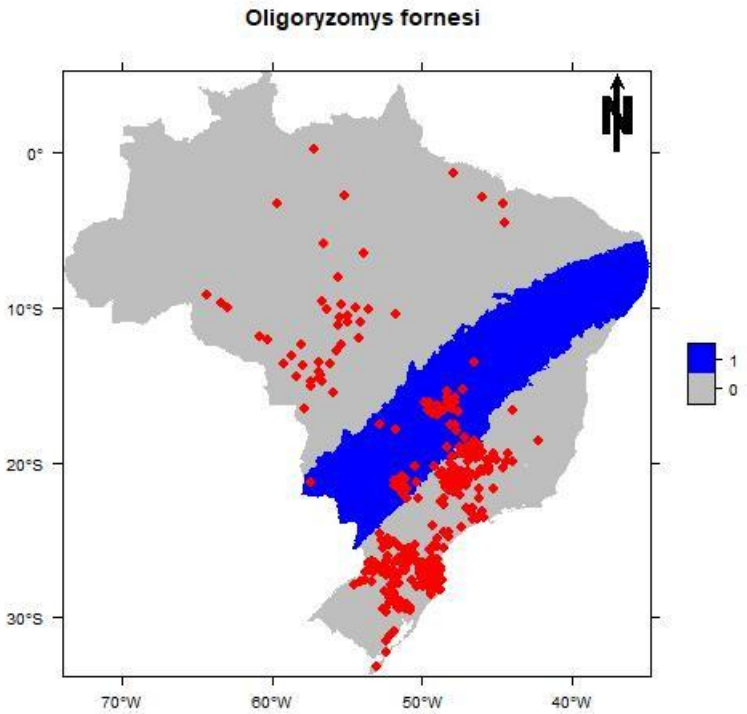

Figure 3-12. Distribution of reservoir rodent species; *Oligoryzomys fornesi*

Note: the blue describe the presence of *Oligoryzomys fornesi* and red dots indicate municipalities with hantavirus report

3.3.2. Variable selection

In terms of land cover variables, some variables were excluded if the proportion of grids which included the land use variables more than 10%, is less than 10%. As Table 3-5 showed, the proportion of grids that have more than 10% of Urban/Built-up was less than 10% (1.29 percent), so it was excluded in the analysis.

Table 3-5. Distribution of land cover variables

Land use	Municipalities of which land use have more than 10%	
	N	%
Forest	4252	76.43
Cultivated and managed vegetation	4589	82.49
Urban/Built-up	72	1.29

Variable excluded: Urban/Built-up (<10%)

The VIF values were also examined to avoid multi-collinearity problems. In the first combination, temperature and latitude showed VIF value higher than 10 (which was a threshold in this study). After excluding latitude which showed the highest VIF value, no variable showed VIF value higher than 10. The process was illustrated in Table 3-6.

Table 3-6. Variable selection process by VIF values

Category	Variables	VIF1	VIF2
Diversity	Rodent richness	2.54	2.56
	Diurnal predator richness	3.16	2.47
	Nocturnal predator richness	5.97	4.34
Forest	Deforestation (2007 – 2014)	1.73	1.69
Socio-demographic variables	Population density (10^3)	1.24	1.24
	% of urban population	1.39	1.38
Economy	Regional GDP per capita (10^3)	1.09	1.09
Climate	Temperature (1990 – 2000)	14.72	7.53
	Precipitation (1990 – 2000)	1.72	1.70
Land use	Forest (%)	4.85	4.57
	Cultivated vegetation (%)	3.42	3.34
Crop production	Corn (10^3)	6.38	6.34
	Soya (10^3)	6.51	6.46
	Sugarcane (10^3)	1.41	1.41
Geography	Elevation	3.70	2.62
	Latitude	14.74	-
	Total space (10^6)	1.84	1.77

Using the VIF values, 16 variables were left and one to one correlation was examined as well, to prevent the multi-collinearity problems. As Figure 3-10 showed, most combinations of variables had low or moderate correlation, but the soya production variable have relatively strong correlation with corn production (0.89). So the soya production variable was excluded.

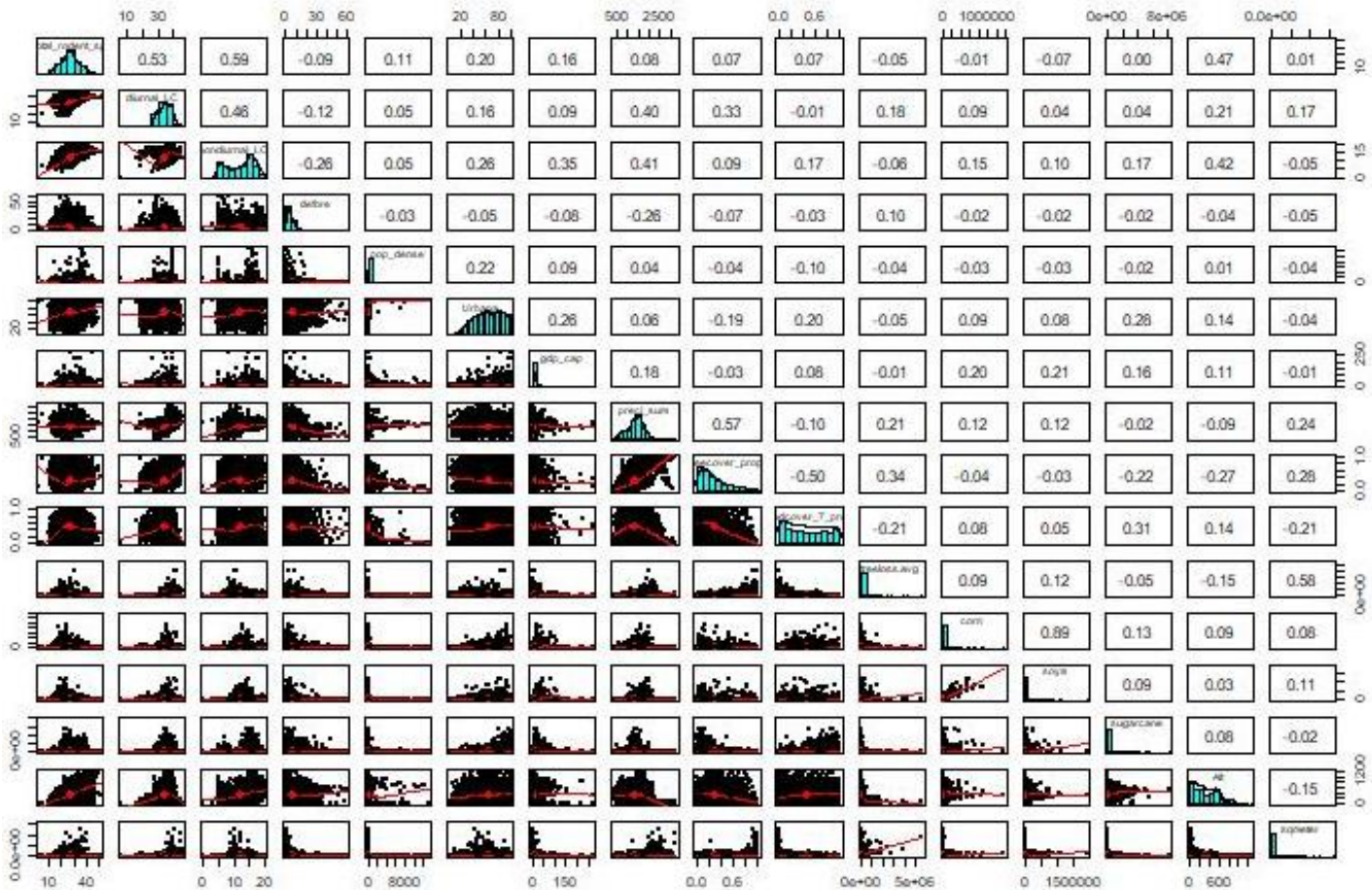

Figure 3-13. One to one correlation of selected variables

3.3.3. Main analysis

Table 3-7 showed the logistic regression results of association between hantavirosis presence and species richness which exclude threatened species. In the final model (model type 3; the model adjusting all the covariates) The association of rodent species richness was significantly negative (OR = 0.906, 95% CI = 0.878 – 0.934), and also diurnal predator species richness (OR = 0.949, 95% CI = 0.907 – 0.993). On the other hand, the association with non-diurnal predator species richness was significantly positive (OR = 1.371, 95% CI = 1.258 – 1.499). AUC value for the final model was 0.861 and DIC was 1999.344. In the Morans' I test for spatial autocorrelation of residuals, the null hypothesis (there was no spatial autocorrelation) was not rejected (I = 0.003, p value = 0.365)

Table 3-7. Analysis results (N = 5,563) – exclude species in threat for predators

Variables	Odds ratio (95% CI)		
	Model type 1	Model type 2	Model type 3
Rodentia	1.031 (1.015 – 1.046)	0.913 (0.890 – 0.936)	0.906 (0.878 – 0.934)
Diurnal	1.066 (1.039 – 1.094)	0.953 (0.923 – 0.985)	0.949 (0.907 – 0.993)
Non-diurnal	1.318 (1.269 – 1.371)	1.218 (1.133 – 1.313)	1.371 (1.258 – 1.499)

Model type 1: Univariate analysis for each species richness variable (model 1-3)

Model type 2: Multivariable analysis for each species richness adjusted by socioeconomic, climate, deforest, land cover, geographic factors (model 4-6)

Model type 3: Multivariable analysis including all species richness adjusted by socioeconomic, climate, deforest, land cover, geographic factors (model 7)

Table 3-8 showed the logistic regression results of association between hantavirosis presence and species richness which include threatened species. In the final model (model type 3; the model adjusting all the covariates) The association of rodent species richness was significantly negative (OR = 0.906, 95% CI = 0.878 – 0.935), and also diurnal predator species richness (OR = 0.948, 95% CI = 0.906 – 0.993). On the other hand, the association with non-diurnal predator species richness was significantly positive (OR = 1.374, 95% CI = 1.262 – 1.500). AUC value for the final model was 0.861 and DIC was 1996.344. In the Morans' I test for spatial autocorrelation of residuals, the null hypothesis (there was no spatial autocorrelation) was not rejected (I = 0.003, p value = 0.348)

Table 3-8. Analysis results (N = 5,563) – including all species of predators

Variables	Odds ratio (95% CI)		
	Model type 1	Model type 2	Model type 3
Rodentia	1.031 (1.015 – 1.046)	0.913 (0.890 – 0.937)	0.906 (0.878 – 0.935)
Diurnal	1.072 (1.046 – 1.099)	0.952 (0.922 – 0.983)	0.948 (0.906 – 0.993)
Non-diurnal	1.322 (1.272 – 1.376)	1.225 (1.140 – 1.320)	1.374 (1.262 – 1.500)

Model type 1: Univariate analysis for each species richness variable (model 1-3)

Model type 2: Multivariable analysis for each species richness adjusted by socioeconomic, climate, deforest, land cover, geographic factors (model 4-6)

Model type 3: Multivariable analysis including all species richness adjusted by socioeconomic, climate, deforest, land cover, geographic factors (model 7)

3.3.4. Sensitivity analysis

Table 3-9 showed the count-based regression model results for examining association between hantavirosis cases and species richness which exclude threatened species. In the final model (NB which showed the lowest DIC) The association of rodent species richness was significantly negative (RR = 0.884, 95% CI = 0.853 – 0.915), and also diurnal predator species richness (RR = 0.934, 95% CI = 0.888 – 0.982). On the other hand, the association with non-diurnal predator species richness was significantly positive (RR = 1.374, 95% CI = 1.252 – 1.513).

Table 3-9. Analysis results (Count based model, N=5,563) – exclude species in threat for predators

Variables	Relative risk (95% CI)			
	Poisson	NB	ZIP	ZINB
Rodentia	0.893 (0.878 – 0.909)	0.884 (0.853 – 0.915)	0.920 (0.898 – 0.942)	0.885 (0.853 – 0.916)
Diurnal (major)	0.964 (0.936 – 0.993)	0.934 (0.888 – 0.982)	0.933 (0.900 – 0.968)	0.934 (0.888 – 0.981)
Non-diurnal (major)	1.296 (1.230 – 1.365)	1.374 (1.252 – 1.513)	1.267 (1.195 – 1.343)	1.373 (1.251 – 1.512)
DIC	4409.702	2985.591	3595.509	2988.040

Multivariable analysis including all species richness adjusted by socioeconomic, climate, deforest, land cover, geographic factors (full model)

Table 3-10 showed the count-based regression model results for examining association between hantavirosis cases and species richness which include threatened species. In the final model (NB which showed the lowest DIC) The association of rodent species richness was negative, but not significant (RR = 0.887, 95% CI = 0.855 – 0.919), and also diurnal predator species richness (RR = 0.932, 95% CI = 0.887 – 0.980). On the other hand, the association with non-diurnal predator species richness was positive but not significant (RR = 1.377, 95% CI = 1.257 – 1.512).

Table 3-10. Analysis results (Count based model, N=5,563) – including all species of predators

Variables	Relative risk (95% CI)			
	Poisson	NB	ZIP	ZINB
Rodentia	0.896 (0.880 – 0.912)	0.887 (0.855 – 0.919)	0.920 (0.898 – 0.943)	0.887 (0.856 – 0.919)
Diurnal	0.953 (0.925 – 0.982)	0.932 (0.887 – 0.980)	0.935 (0.902 – 0.970)	0.932 (0.887 – 0.980)
Non-diurnal	1.324 (1.257 – 1.394)	1.377 (1.257 – 1.512)	1.273 (1.202 – 1.350)	1.375 (1.256 – 1.511)
DIC	4390.733	2982.826	3590.616	2985.320

Multivariable analysis including all species richness adjusted by socioeconomic, climate, deforest, land cover, geographic factors (full model)

3. 4. Discussion

Throughout this study, I investigated the association between predator species richness and endemic hantavirosis incidence in Brazil under the hypothesis that the high species richness of predator may chronically suppress the population dynamics in reservoir rodent population and subsequently reduce the risk of spill over to human population. The results showed that species richness of diurnal predators had a statistically significant negative association with hantavirosis notification in the best fitting model of both binary and count-based models, whereas the association with nocturnal predators' species richness was positively significant in the best fitting models.

While there is no definitive evidence supporting that *Necromys lasiurus* is the most dominant reservoir species in Brazil, several field survey revealed that relative population of *N. lasiurus* was higher than other species in some local regions (116, 117), and the data used in this study also showed the consistency (Appendix 3-3). In this regards, the significant associations of diurnal predator species richness would be explained by the regulatory pressure of diurnal predators on diurnal dominant species. On the other hands, the positive association with non-diurnal predator also fit into the hypothesis, in that the nocturnal predators chronically suppress population of nocturnal rodents, which consisted of higher number of species than diurnal, the decreased competitor would increase habitat suitability of diurnal rodent species in indirect ways.

The sensitivity analysis revealed that the regulatory role of predator species richness was maintained even when including predator species which are in the threat of extinction, representing lower level of population size, or decreasing trend of population. The results implied that extinction of these species may increase the risk of human RBDs by decreased level of regulatory pressures from them.

There are several limitations which should be considered for proper interpretation. First, the study did not consider the changes of species richness in the study period (2006 – 2016). Although the species distribution map from IUCN and birdlife has been updated regularly with description of updated years, systematic or real time assessment is too demanding to be realized. But the limitation would be solved in the further studies by employing previous version of IUCN data as the study from Betts et al (48). Second, the other species which is not incorporated in this study may affect the association. For example, there are several species in insectivore which are in the same trophic hierarchy as rodents could limit the rodent population as competitors. Third, the effect of evenness of wildlife cannot be examined, as the population size data for each species was not possible to obtain however it would have effects on the hantavirosis transmission as well. Although there has been several field survey on a local-level in Brazil, systematic survey that cover all country by using cutting edge technique would be beneficial not only for ecological study and also public health purpose. Fourth, the study unit, municipality was used in this study, would affect the results, in that different scale of study unit (e.g, $1km^2$ grid) would

produce different sample size and values in explanatory variables (Modifiable area unit problem, MAUP).

Nevertheless, the study results had important implication on both public health and wildlife conservation. In the human public health perspectives, the founded association could be applied to predict the risk areas considering the fluctuation of species richness. Moreover, because the increasing predator species richness could be a practical intervention, fundamental and pre-emptive countermeasures with ecological point of view would be designed and developed with collaboration of environmental departments. Furthermore, the study results support the need of wildlife conservation with utilitarian point of view which may facilitate advocating publics and political changes.

Chapter IV.

Predator's regulation on endemic HFRS incidence in South Korea

4.1. Introduction

4.1.1. Impact of hanta virus in Korea

Since the first hemorrhagic fever with renal syndrome (HFRS) outbreak was reported during the Korean war (118), the endemic diseases has persistently caused public health issues and the number of cases has even increases recently. As a rodent-borne disease, which can be transmitted from natural rodent reservoirs (119), mainly *Apodemus agrarius* in South Korea, minimizing the contact to rodents has been considered as one of the most effective prevention strategies.

The fatality rate is ranged 1.5% to 12% for Hantaan virus and relatively lower for Seoul virus as less than 1% (120). However, the number of incidence cases has persistent despite all the campaigns and warnings from local public health centers, and recently increased to more than 500 cases (Figure 4-1).

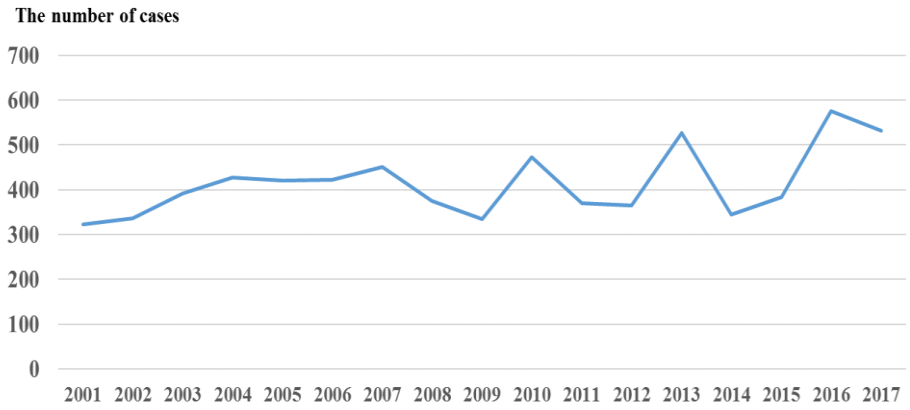

Figure 4-1. The number of annual HFRS reported cases from 2001 to 2017

4.1.2. Previous studies on hantavirus in Korea

A number of studies reported a various possible risk factors. Xiao et al (121) suggested that present of local rodent reservoir, meteorological factors, geographic factors (normalized difference vegetation index, NDVI), and economic status were significantly associated with HFRS incidence in China. Tian et al (122) reported U-shape association between urbanization and HFRS incidence. Joshi et al (123) reveals the significant role of climate factors on HFRS incidence in Korea.

The role of wildlife rather than just existence of reservoir rodents, however, has not been well documented relatively. Although many types of studies including field experiment, observational studies and theoretical mathematical modelling studies have elaborated the association between wildlife diversity and RBDs, no evidence has been reported in Korea, which presented relatively low wildlife diversity and suffered diversity loss for decades due to massive habitat destruction and degradations (124)

4.1.3. Goal of study & study design

In this chapter, the association of wildlife diversity with HFRS incidence was investigated to examine dilution effect and also the effect of predators' diversity including both mammals (Carnivore) and avian species (Accipitridae, Falconidae and Strigidae).

In terms of species richness, three variables were employed as the major explanatory factors; rodent species richness, diurnal predator species richness and non-diurnal predator species richness. The rodent species richness was incorporated to investigate whether the dilution effect works for preventing HFRS incidence in Korea, and the predator species richness was included to examine the suppression effect of predators on the spill-over event.

Supposing that the effect size of diurnal predators' regulation on the diurnal reservoir and that of nocturnal predators on the nocturnal reservoirs would be different, the effects of diurnal and nocturnal predators were discretely tested. In addition, species which were under threat of extinction were not included in the main analysis, because species with relatively lower population would not be influential enough. To this end, species categorized as "Least Concern (LC)" or "Near threatened (NT)" by IUCN (62) were included and the others ("Vulnerable (VN)", "Endangered (EN)", "Critically Endangered (CR)") were excluded in this study.

4.2. Materials and methods

4.2.1. Data acquisition

To examine the study hypothesis, various types of data representing Hantavirosis outbreak (main outcome), species richness of wildlife (main explanatory variables), and other covariates, including anthropogenic, climate, land cover, and geographic factors, were needed. Although there was no single source of database that collected all of these variables systematically, the feature of spatial data that can be merged based on common spatial locational attributes, enables to comprehensively utilize a number of data from various sources (Table 4-1).

4.2.1.1. Hantavirosis incidence

The number of HFRS cases was obtained from infectious disease portal from Korean Center for Disease Control and Prevention (KCDC). They provided the annual number of cases by sex and age groups in national level and also by second administrative levels (sigungu). All data is fully open access that does not require any permissions

4.2.1.2. Wildlife species richness

There are global level spatial data from IUCN that represent the geographic range of each mammalian species (62), but this would not be suitable for the studies

of which study background is Korea, because Korea is relatively small country and the IUCN data may not sophisticatedly capture the delicate differences between sigungu areas. In this regard, species occurrence reports from national ecosystem survey (125) conducted by National Institute of Ecology (NIE) was used. The survey was implemented from 2006 and ended 2012.

4.2.1.3. Sociodemographic factors

Total population size and the number of farmers were obtained from Korean Statistical Information Service (KOSIS). The data was provided by year and by sigungu. The population size by each sex and age group was also obtained from the same data source which was used to calculate expected number of HFRS cases.

4.2.1.4. Meteorological factors

Meteorological factors, including annual average temperature, annual average relative humidity, total sunlight time and total precipitation, were obtained from Korea Meteorological Administration' automatic synoptic observation system (ASOS) (126), which is fully open access from its web site. The data was provided by each observation site with their location information (coordinates).

4.2.1.5. Land cover and deforestation

As a proxy of land cover change, deforestation data from Global Forest Change (GFC) (76) was incorporated.

4.2.1.6. Geographic factors

Elevation data was obtained from David et al (112) which provided 1km scale global elevation data. Although there have been various altitude data that presented more fine scale, such 30m, the lower resolution map was selected to minimize computational burden. On the other hands, total extent of each sigungu area was directly obtained from the KOSIS web site (127).

Table 4-1. Data acquisition

Category1	Category 2	Variables	Data source	ref
Response variable	Outcome	Hantavirosis incidence	KCDC	(128)
Main explanatory variables	Wildlife diversity	Rodentia	NIE*	(125)
		Carnivora	NIE	
		Raptors	NIE	
		Strigidae	NIE	
Covariates	Deforestation	Treeloss	GFC	(76)
	Socio-demography	Population	KOSIS	(127)
		% of farmers	KOSIS	
		Household	KOSIS	
		Male pop.	KOSIS	
		Farmer pop (male)	KOSIS	
	Economy	Budget dependency	KOSIS	
	Meteorology	Average temperature	KMA ASOS	(126)
		Precipitation	KMA ASOS	
		Relative humidity	KMA ASOS	
		Sunlight total time	KMA ASOS	
	Landuse	Agriculture (paddy)	KOSIS	
		Agriculture(field)	KOSIS	
		Agriculture (All)	KOSIS	
		Urbanicity (%)	KOSIS	
		Treecover	GFC	
	Geography	Elevation	GLOBE	(112)
		Extent	KOSIS	

NIE: National Institute of Ecology

4.2.2. Data preprocessing

Data preprocessing has been conducted to create dataset for the analysis from spatial data.

4.2.2.1. Expected number of HFRS incidence

As the number of HFRS cases was obtained by table format directly from KOSIS, data preprocessing was not required. But the expected number of HFRS cases was calculated from the total number of cases by sex and age groups and sex and age structure of each sigungu.

4.2.2.2. Administrative region standardization

During the target study period, from 2006 to 2016, the number of sigungu has fluctuated almost every year. For example, Sejong-si was newly introduced in the region, previously named yeongi-gun. Considering that the main explanatory variable, species occurrence data, was provided by sigungu categorization in 2016 (N=250), the sigungu categorization should be standardized to fit that of 2016. The detailed process was described in Appendix 4-1.

4.2.2.3. Wildlife species richness

NIE provided the database of species occurrence by table format. Although the data included the list of all species (including mammals, avians, reptiles and amphibians) observed in each sigungu, only species in the category of Accipitridae, Falconidae, Strigidae, Carnivore (as predator species), and Rodentia were extracted. Each species extracted was additionally examined its circadian characteristics (whether it is nocturnal or diurnal) and its preference on rodent prey (to exclude obligate predator for aquatic prey). All examination was based on published literature or web based database.

4.2.2.4. Socio-demographic factors

As the data from KOSIS was obtained by table format, no preprocessing was required. But the data from 2006 to 2015 was modified to fit the standardized administrative regions as described in the previous section.

4.2.2.5. Meteorological factors

As the meteorological data was obtained for each observation site by point format, the data did not represent each sigungu. To elicit representative value for each sigungu, ordinary kriging was employed which is one of spatial interpolation method.

With this method, raster type meteorological data was generated and then extracted by administrative borderlines.

4.2.2.6. Land cover and deforestation

To assess deforestation, I used both forest cover in 2000 and treeloss events from GFC database (76) The forest cover variable was in the format of raster and values ranged from 0 to 100 representing the probabilities of tree canopy presence. As a previous study employed (48) I used 75 as threshold to define forest presence. Subsequently, the treeloss variable, of which format was raster and values are binary, was calculated by product of preprocessed forest present variables and treeloss variables, to count tree loss event only in the presence of forest. These process was followed by a previous study (48)

4.2.2.7. Geographic factors

The elevation variables were provided with raster format, and I used 'getValues' functions to extract and averaging the values in the raster cells to generate data for each municipality polygon.

Table 4-2. Data preprocessing

Category	Variables	Data type	Preprocessing
Outcome	Hantavirosis incidence	Tables	No needed
Wildlife diversity	Rodentia	Vectors	Intersection
	Carnivora	Vectors	No needed
	Raptors	Vectors	No needed
	Strigidae	Vectors	No needed
Deforestation	Treeloss	Raster	Extraction
Socio-demography	Population	Tables	No needed
	% of farmers	Tables	No needed
	Household	Tables	No needed
	Male pop.	Tables	No needed
	Farmer pop (male)	Tables	No needed
Economy	Budget dependency	Tables	No needed
meteorology	Average mean temperature	Vectors	Ordinary kriging
	Precipitation	Vectors	Ordinary kriging
	Relative humidity	Vectors	Ordinary kriging
	Sunlight total time	Vectors	Ordinary kriging
Landuse	Agriculture (paddy)	Tables	No needed
	Agriculture(field)	Tables	No needed
	Agriculture (All)	Tables	No needed
	Urbanicity (%)	Tables	No needed
	Treecover	Raster	Extraction
Geography	Elevation	Raster	Extraction
	Extent	Tables	No needed

4.2.3. Statistical analysis

Descriptive analysis was conducted to overview the difference between districts with higher incidence of HFRS cases and with lower incidence from 2006 to 2016 based on the median value. Mean and standard deviation were provided, and choropleth maps with decile values were also shown to assist understanding of the spatial distributions.

As suggested in the previous section, the variables in this study, specifically, covariates, were included based on the previous finding that both outcome and main explanatory variables were affected, which is not model-based approach. However, not all covariate was included and variable selection process was implemented to avoid multi-collinearity issue. As previous studies suggested, variables with higher than VIF value 10 (87) and one to one correlation coefficients more than 0.8 were excluded.

Four count-based models; poisson, negative binomial (NB), zero-inflated poisson (ZIP), zero-inflated negative binomial (ZINB), were employed to examine the associations. A main model included all covariates and all species richness, but unadjusted models were also fitted for the best fit model, in order to compare the results with the adjusted models. Considering that the possible autocorrelation of residuals by time (year) and space, hierarchical approaches were also incorporated (91). For Bayesian inference, integrated nested Laplace approximation (INLA) approaches (129) has been employed by INLA package (90) in R v. 3.5.0 (78). Results from all models were described with relative risk (RR) and 95% credible interval (95%

CI). Goodness of fit was examined for all regression models by Deviance information criterion (DIC) (88) value also provided.

4.3. Results

4.3.1. Descriptive analysis

The overall descriptive information was presented in Table 4-3. The species richness of rodents, diurnal predators, and nocturnal predators are higher in the regions with higher HFRS notification cases (as 4.68, 4.31 and 4.15 respectively) than non-outbreak regions (the species richness was 3.33, 2.98 and 3.13 respectively). Population density was also lower in the high incidence regions (2.64 thousand per km^2) than the others (5.41 thousand per km^2). In terms of meteorological factors, regions with high hantavirosis notification showed slightly higher precipitation level (1306.5 mm) than the others (1305.2 mm), but the temperature was slightly higher in lower incidence area (12.9 degree) than the others (12.7 degree).

The 3 land use variables, including forest, agriculture and urban area were higher in the high incidence area (212.8 km^2, 9999.9m^2, 82.4km^2, respectively) than the other sigungu (207.6 km^2, 3715.1m^2, 56.4km^2, respectively). In terms of elevation, high risk areas showed lower (153.2 m) than lower risk areas (187.3 m)

Table 4-3 Descriptive analysis

Category1	Category 2	Variables	Mean (±SD)	
			Higher HFRS (>median, N = 124)	Lower HFRS (≤median, N = 126)
Response variable	Outcome	HFRS incidence cases (annual mean; 2006 - 2016)	30.21 ± 19.7	6.13 ± 3.0
Main explanatory variables	Species richness	Rodents	4.68 ± 1.3	3.33 ± 2.2
		Diurnal predator	4.31 ± 2.7	2.98 ± 3.1
		Non-diurnal predator	4.15 ± 1.8	3.13 ± 2.2
Covariates	Deforestation	Deforestation (2006-2016, sum, km^2)	7.28 ± 9.0	4.70 ± 8.9
	Demography	Population density (10^3 per km^2)	2.64 ± 5.1	5.41 ± 6.9
	Economy	Budget dependency (%)	26.93 ± 14.6	32.02 ± 17.6
	meteorology	Average mean temperature (C)	12.73 ± 0.9	12.86 ± 1.2
		Precipitation (mm)	1306.47 ± 105.9	1305.22 ± 139.4
		Relative humidity (%)	68.85 ± 2.6	66.91 ± 2.3
		Sunlight total time (hour)	2104.92 ± 33.0	2122.21 ± 28.2
	Landuse	Agriculture (paddy, m^2)	6299.2 ± 5763.8	1538.5 ± 2343.4
		Agriculture (All, m^2)	9999.9 ± 7956.0	3715.1 ± 5419.4
		Urbanicity (km^2)	82.44 ± 80.2	56.39 ± 71.8
		Treecover (km^2)	212.78 ± 236.8	207.56 ± 326.8
	Geography	Elevation (mean, m)	153.22 ± 119.36	187.25 ± 172.98
		Extent (km^2)	488.72 ± 338.8	317.63 ± 389.2

*HFRS: Hemorrhagic fever with renal syndrome

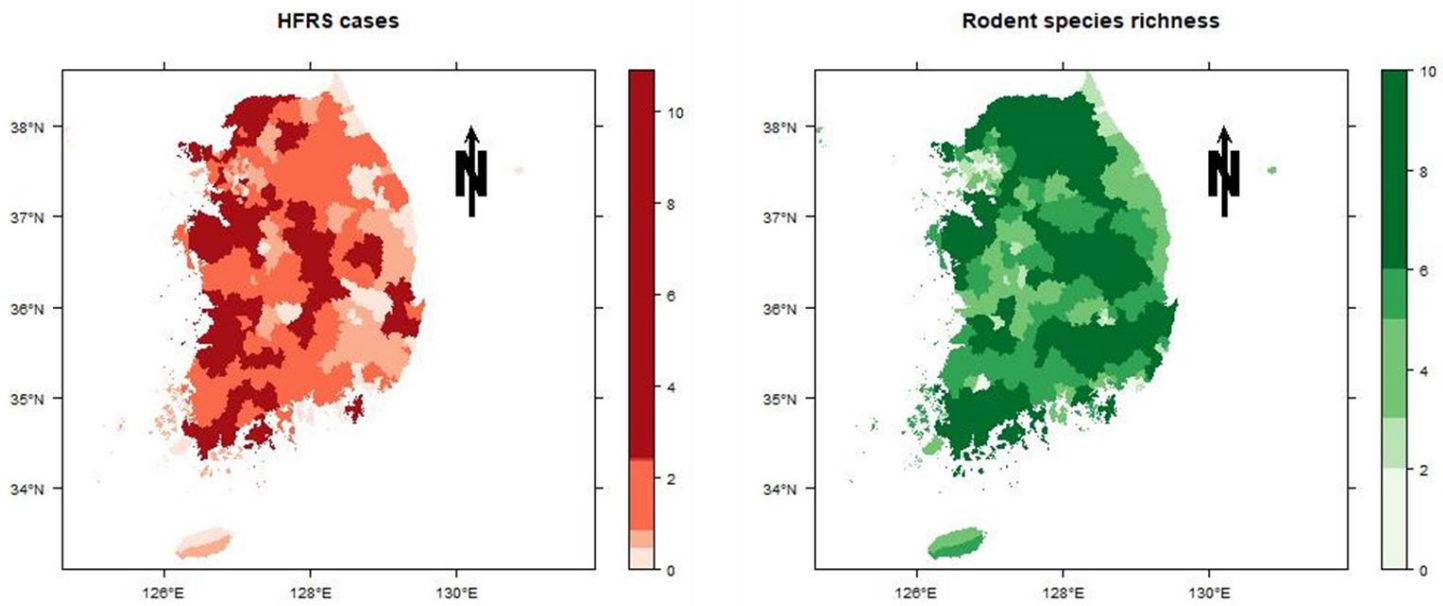

Figure 4-2. Distribution of HFRS cases between 2006 - 2016 (left) and rodent species richness (right)

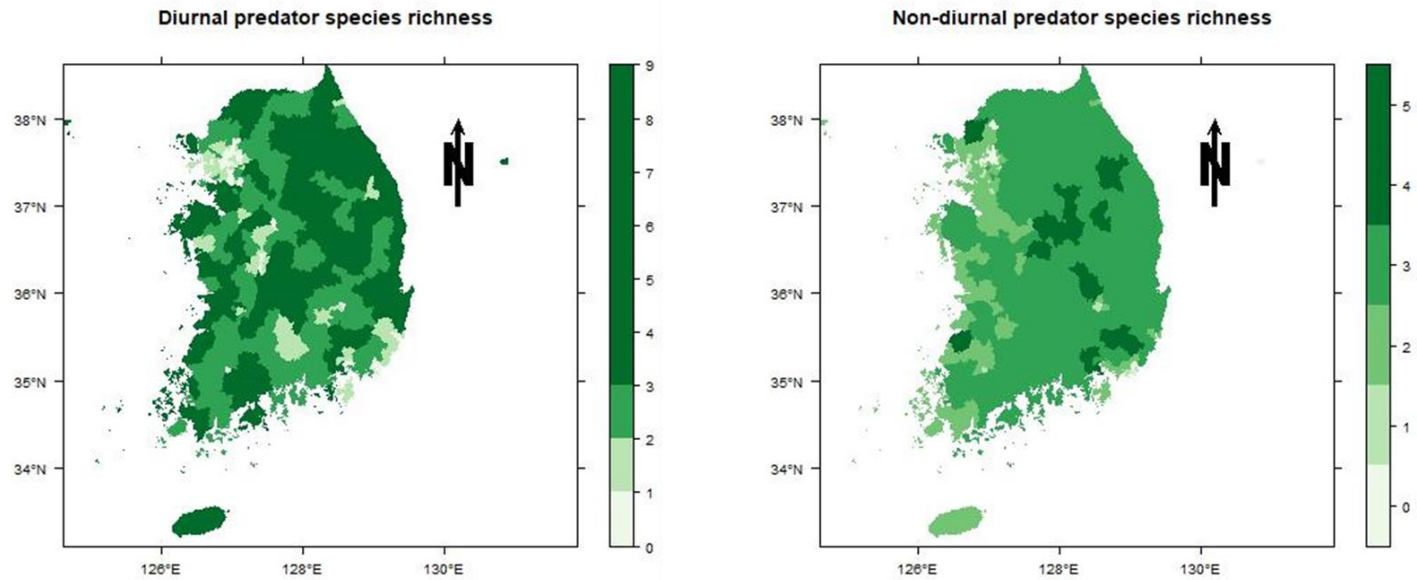

Figure 4-3. Distribution of diurnal predator species richness (left) and non-diurnal predator species richness (right)

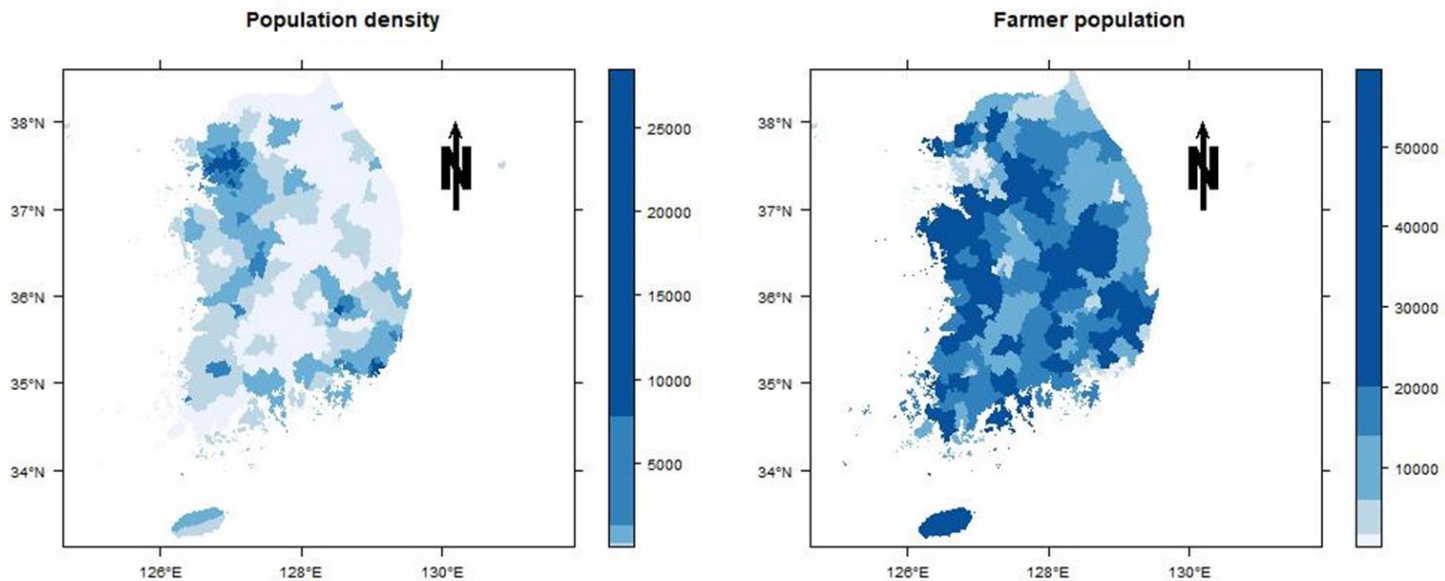

Figure 4-4. Distribution of diurnal population density (left) and farmer population (right)

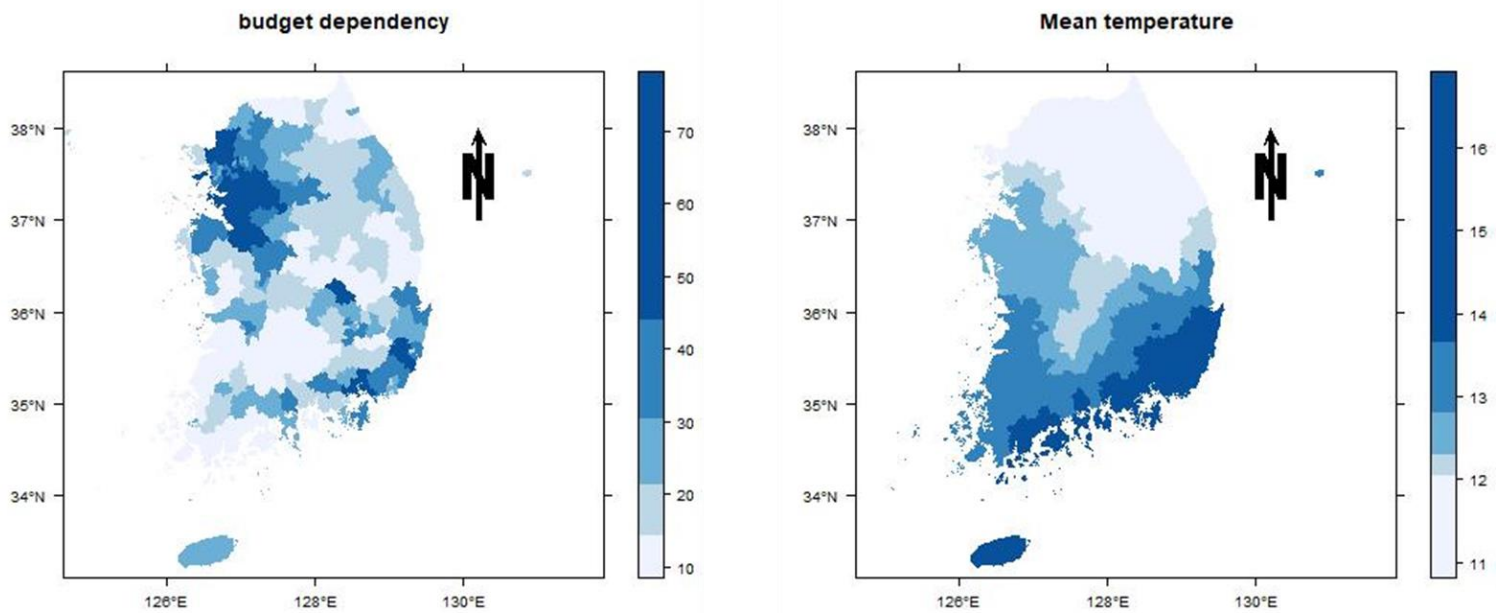

Figure 4-5. Distribution of budget dependency (left) and annual mean temperature (right)

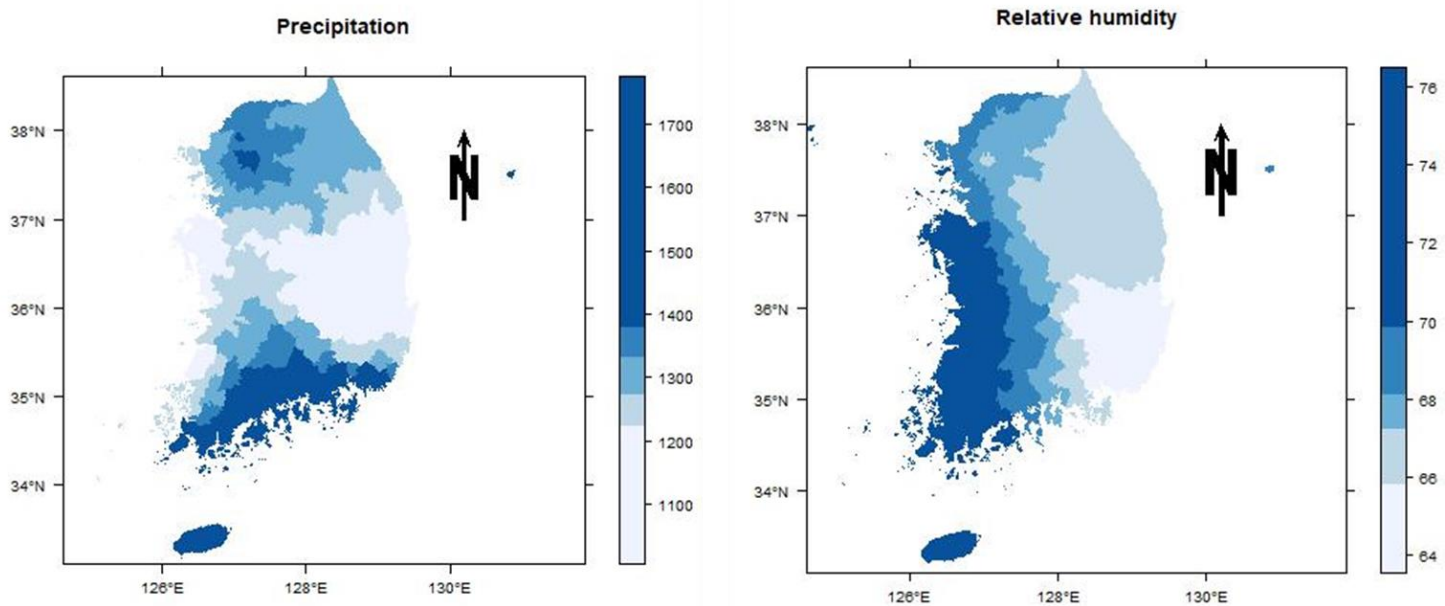

Figure 4-6. Distribution of annual total precipitation (left) and relative humidity (right)

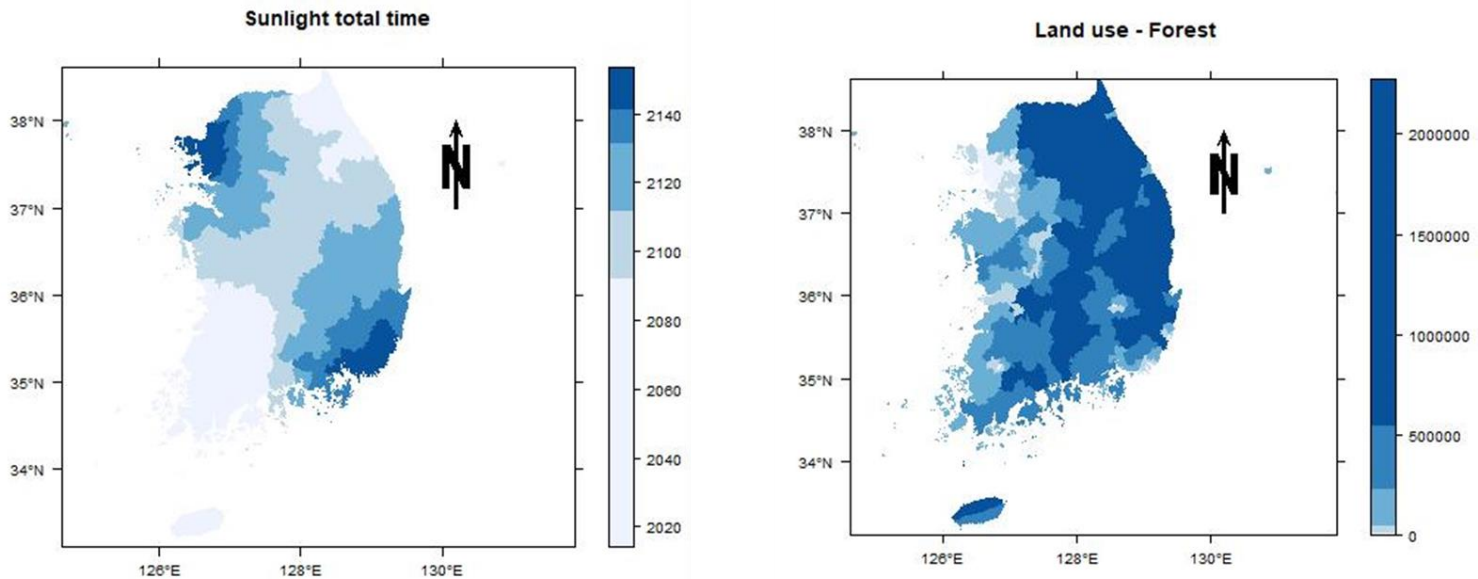

Figure 4-7. Distribution of annual sunlight total time (left) and Forest land cover (right)

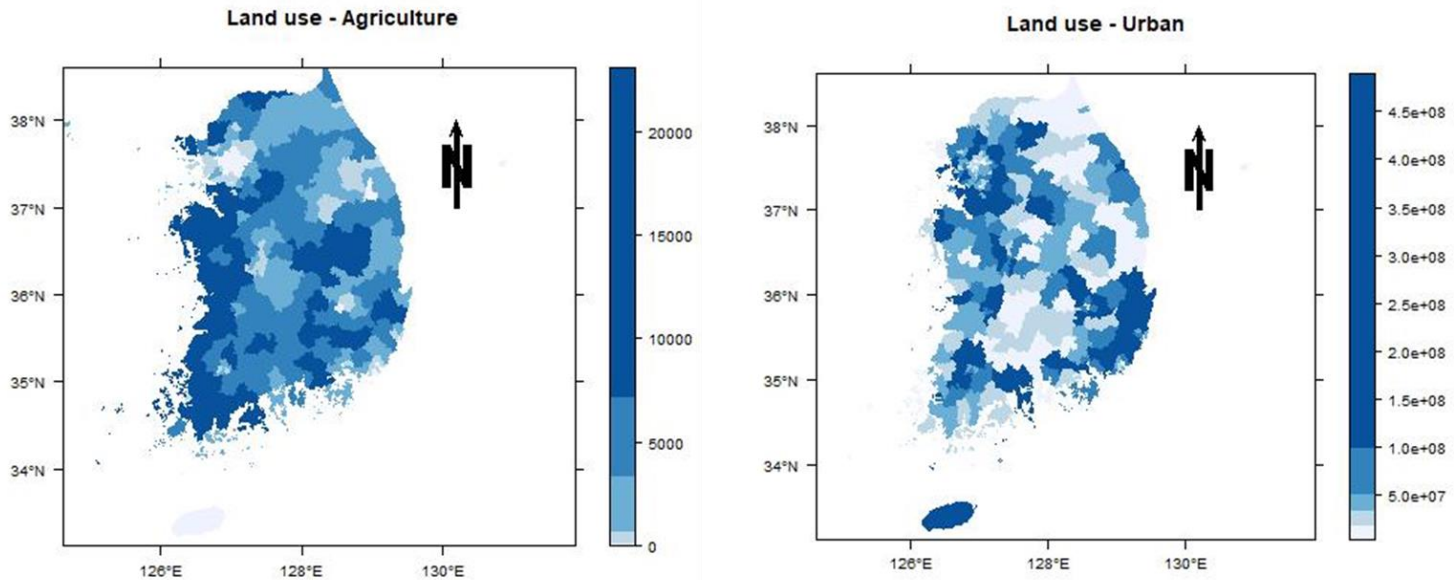

Figure 4-8. Distribution of agriculture land use (left) and urban land use (right)

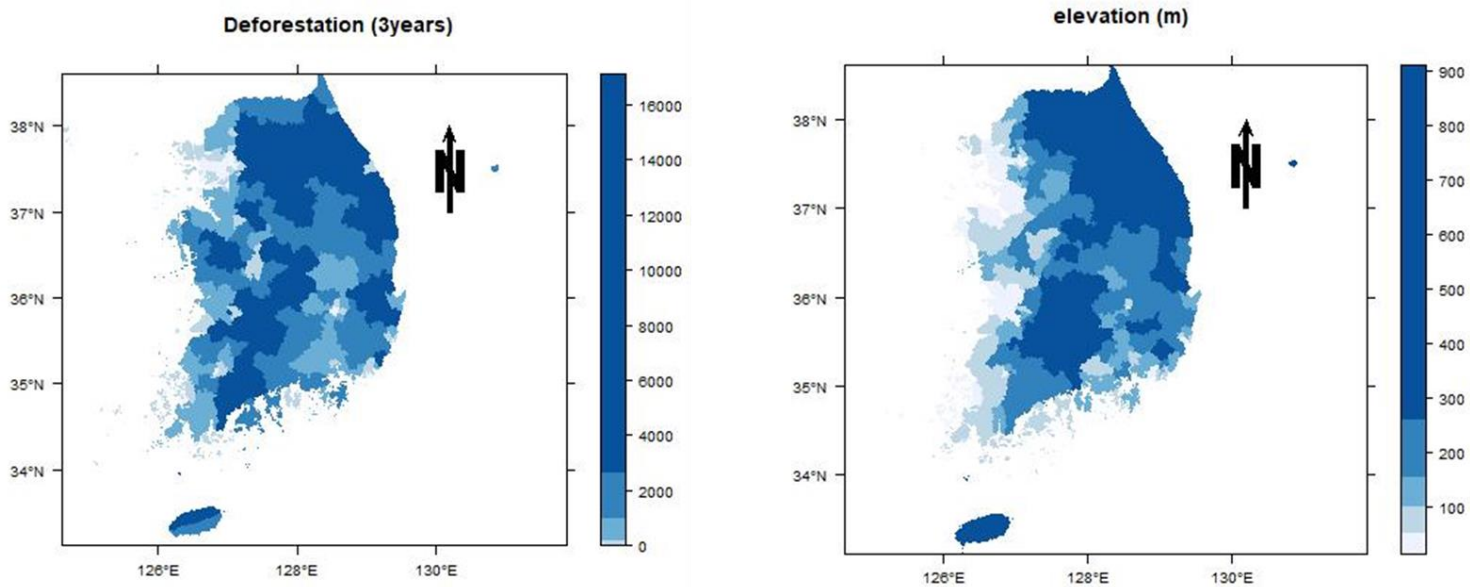

Figure 4-9. Distribution of deforestation (left) and elevation (right)

4.3.2. Variable selection

The VIF values were also examined to avoid multi-collinearity problems. In the first combination, agricultural land use (paddy field) and agricultural land use (total), land cover of forest, and total extent showed VIF value higher than 10 (which is a threshold in this study). After excluding total size of sigungu, which showed the highest VIF value, two agricultural landuse variable showed VIF values higher than 10. After excluding all agricultural land use which showed higher value, no variable showed VIF value higher than 10. The process was illustrated in Table 4-4.

Table 4-4. Variable selection

Category	Variables	VIF1	VIF2	VIF3
Species richness	Rodents	2.32	2.16	2.13
	Diurnal predator	2.21	2.05	1.90
	Non-diurnal predator	2.14	2.02	2.02
Deforestation	Treeloss (3 years)	2.22	2.29	2.25
Socio-demography	Population density	2.32	2.29	2.27
	Farmers	5.52	5.37	3.37
Economy	Budget dependency (%)	2.45	2.40	2.39
meteorology	Average mean temperature	1.67	1.42	1.39
	Precipitation	1.32	1.29	1.29
	Relative humidity	1.77	1.76	1.69
	Sunlight total time	1.32	1.31	1.29
Landuse	Agriculture (paddy)	12.68	11.42	4.46
	Agriculture (All)	24.79	18.35	-
	Urbanicity (km^2)	1.68	1.66	1.62
	Treecover	20.89	4.91	4.79
Geography	Elevation (mean, m)	4.44	4.32	4.28
	Extent (km^2)	29.95	-	-

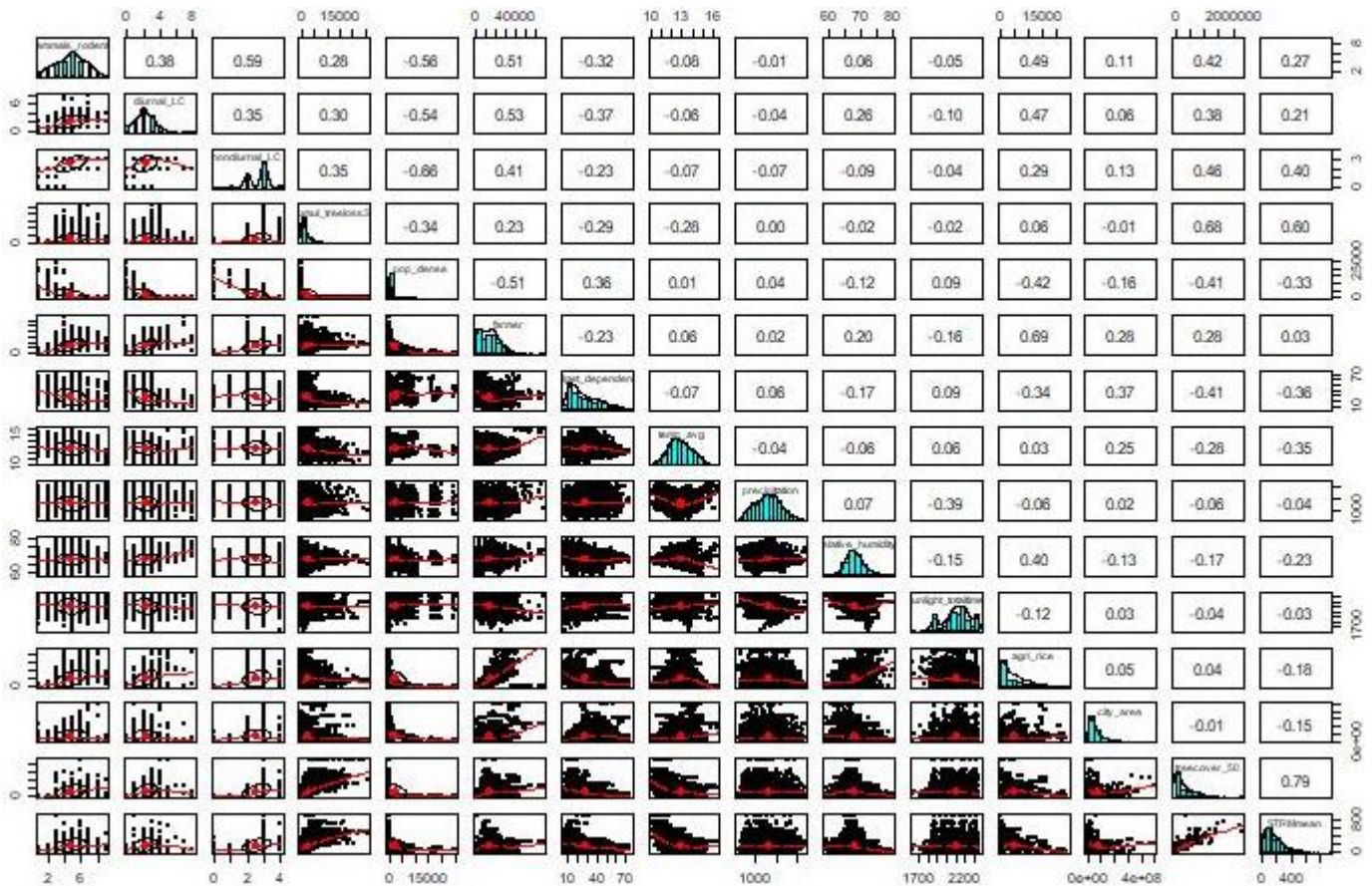

Figure 4-10. One to one correlation of selected variables

4.3.3. Main analysis

Table 4-5 showed the count-based regression model results for examining association between HFRS cases and species richness which exclude threatened species. In the final model (NB which showed the lowest DIC) The association of rodent species richness was significantly positive (RR = 1.131, 95% CI = 1.088 – 1.177). On the other hand, both diurnal and non-diurnal predator species richness showed negative association which is significant (RR for diurnal predators = 0.942, 95% CI = 0.895 – 0.991; RR for non-diurnal predators = 0.886, 95% CI = 0.807 – 0.972).

Table 4-5. Analysis results (Non-spatial model)

Variables	Relative risk (95% CI)			
	Poisson	NB	ZIP	ZINB
Rodentia	1.141 (1.113 – 1.169)	1.131 (1.088 – 1.177)	1.144 (1.115 – 1.173)	1.132 (1.088 – 1.177)
Diurnal	0.926 (0.898 – 0.954)	0.942 (0.895 – 0.991)	0.945 (0.915 – 0.975)	0.942 (0.896 – 0.992)
Non-diurnal	0.868 (0.818 – 0.922)	0.886 (0.807 – 0.972)	0.871 (0.818 – 0.927)	0.885 (0.807 – 0.972)
DIC	8721.881	7556.051	8412.405	7558.777

Multivariable analysis including all species richness adjusted by anthropogenic, climate, forest, land cover, geographic factors (full model)

Posterior mean of the over-dispersion parameter and 95% credible interval

zero-probability parameter

Table 4-6 showed the count-based regression model results for examining association between HFRS cases and species richness which exclude threatened species. In the final model (NB which showed the lowest DIC) The association of rodent species richness was positive but contained one (RR = 1.071, 95% CI = 0.997 – 1.150). On the other hand, both diurnal and non-diurnal predator species richness showed negative association but only diurnal predators was significant (RR = 0.899, 95% CI = 0.826 – 0.975) not with non-diurnal predators (RR = 0.995, 95% CI = 0.841 – 1.181). The DIC value is lower in the spatial model indicating better fit was achieved with consideration of space and time autocorrelation.

Table 4-6. Analysis results (Spatial model)

Variables	Relative risk (95% CI)			
	Poisson	NB	ZIP	ZINB
Rodentia	1.070 (0.992 – 1.153)	1.071 (0.997 – 1.150)	1.066 (0.989 – 1.149)	1.071 (0.993 – 1.154)
Diurnal	0.909 (0.831 – 0.993)	0.899 (0.826 – 0.975)	0.904 (0.827 – 0.987)	0.902 (0.825 – 0.983)
Non-diurnal	0.982 (0.822 – 1.176)	0.995 (0.841 – 1.181)	0.989 (0.828 – 1.182)	0.994 (0.833 – 1.189)
DIC	7553.580	7144.634	7452.963	7145.259

Multivariable analysis including all species richness adjusted by anthropogenic, climate, forest, land cover, geographic factors (full model)

Table 4-7. Analysis results – Negative binomial (Non-spatial model)

Variables	Relative risk (95% CI)		
	Model type 1	Model type 2	Model type 3
Rodentia	1.350 (1.309 – 1.393)	1.117 (1.076 – 1.160)	1.131 (1.088 – 1.177)
Diurnal	1.374 (1.309 – 1.443)	0.934 (0.888 – 0.984)	0.942 (0.895 – 0.991)
Non-diurnal	1.514 (1.398 – 1.640)	0.965 (0.882 – 1.055)	0.886 (0.807 – 0.972)

Model type 1: Univariate analysis for each species richness variable (model 1-3)

Model type 2: Multivariable analysis for each species richness adjusted by anthropogenic, climate, forest, land cover, geographic factors (model 4-6)

Model type 3: Multivariable analysis including all species richness adjusted by anthropogenic, climate, forest, land cover, geographic factors (model 7)

Table 4-8. Analysis results – Negative binomial (Spatial model)

Variables	Relative risk (95% CI)		
	Model type 1	Model type 2	Model type 3
Rodentia	1.247 (1.164 – 1.336)	1.082 (1.008 – 1.163)	1.071 (0.997 – 1.150)
Diurnal	1.019 (0.913 – 1.134)	0.887 (0.815 – 0.964)	0.899 (0.826 – 0.975)
Non-diurnal	1.385 (1.149 – 1.671)	1.038 (0.874 – 1.233)	0.995 (0.841 – 1.181)

Model type 1: Univariate analysis for each species richness variable (model 1-3)

Model type 2: Multivariable analysis for each species richness adjusted by anthropogenic, climate, forest, land cover, geographic factors (model 4-6)

Model type 3: Multivariable analysis including all species richness adjusted by anthropogenic, climate, forest, land cover, geographic factors (model 7)

4. 3. 4. Sensitivity analysis

Table 4-9 showed the count-based regression model results for examining association between HFRS cases and species richness which include threatened species. In the final model (NB which showed the lowest DIC) The association of rodent species richness was significantly positive (RR = 1.130, 95% CI = 1.086 – 1.175). On the other hand, both diurnal and non-diurnal predator species richness showed negative association but only diurnal predators was significant (RR = 0.964, 95% CI = 0.937 – 0.991) not with non-diurnal predators (RR = 0.975, 95% CI = 0.926 – 1.027).

Table 4-9. Analysis results (Non-spatial model)

Variables	Relative risk (95% CI)			
	Poisson	NB	ZIP	ZINB
Rodentia	1.132 (1.105 – 1.160)	1.130 (1.086 – 1.175)	1.136 (1.108 – 1.165)	1.130 (1.086 – 1.175)
Diurnal	0.935 (0.937 – 0.969)	0.964 (0.937 – 0.991)	0.962 (0.945 – 0.979)	0.964 (0.937 – 0.991)
Non-diurnal	0.980 (0.948 – 1.013)	0.975 (0.926 – 1.027)	0.966 (0.933 – 1.001)	0.975 (0.926 – 1.027)
DIC	8727.141	7559.604	8415.134	7562.312

Multivariable analysis including all species richness adjusted by anthropogenic, climate, forest, land cover, geographic factors (full model)

Table 4-10 showed the count-based regression model results for examining association between HFRS cases and species richness which include threatened species. In the final model (NB which showed the lowest DIC) The association of rodent species richness was positive but contained one (RR = 1.068, 95% CI = 0.994 – 1.147). On the other hand, both diurnal and non-diurnal predator species richness showed negative association which is not significant (RR for diurnal predators = 0.942, 95% CI = 0.897 – 0.988; RR for non-diurnal predators = 1.088, 95% CI = 0.990 – 1.199). The DIC value is lower in the spatial model indicating better fit was achieved with consideration of space and time autocorrelation.

Table 4-10. Analysis results (Spatial model)

Variables	Relative risk (95% CI)			
	Poisson	NB	ZIP	ZINB
Rodentia	1.065 (0.989 – 1.146)	1.068 (0.994 – 1.147)	1.059 (0.986 – 1.138)	1.068 (0.991 – 1.151)
Diurnal	0.936 (0.889 – 0.984)	0.942 (0.897 – 0.988)	0.929 (0.885 – 0.974)	0.944 (0.896 – 0.993)
Non-diurnal	1.098 (0.994 – 1.216)	1.088 (0.990 – 1.199)	1.115 (1.014 – 1.228)	1.083 (0.979 – 1.201)
DIC	7566.034	7142.127	7451.502	7141.815

Multivariable analysis including all species richness adjusted by anthropogenic, climate, forest, land cover, geographic factors (full model)

4. 4. Discussion

In this chapter, I purposed to investigate the association between predator species richness and endemic HFRS incidence in South Korea under the hypothesis that the high species richness of predator may chronically suppress the population dynamics in reservoir rodent population and subsequently reduce the risk of spill over to human population. The results showed that species richness of diurnal predators had a statistically significant association with HFRS incidence in both non spatial and spatial model, whereas the association with non-diurnal predators' species richness was not significant in the spatial model.

Considering the NB model with spatiotemporal autocorrelation as the best fitting models, based on DIC value, the associations were consistent with the hypothesis as described. Although there could be other possible explanation for the significant finding, these supported the regulatory role of predator species richness on rodent population dynamics. However, the finding could be difficult to generalize in other ecological context, since the reason that the association was significant would be because the reservoir rodent of HFRS is dominant species, consisting of about 80% of total rodent population in Korea. Although it is not confirmed in ecological context, a microorganism level study found that the diversity of predator could increase the predation pressure which is independent to density, and the predator pressure could affect more on dominant species that the others.

The sensitivity analysis revealed that the regulatory role of predator species richness was still consistent when including predator species in the threat of

extinction. It represented that even predator species which in the lower level of population size, or decreasing trend of population would have an important role for the prevention, implying that current wildlife conservation interventions from environmental sectors would be beneficial to public health as well.

There are several limitations which should be considered for proper interpretation. First, the study did not consider the changes of species richness in the study period (2006 – 2016). Considering that the survey of wildlife species occurrence took multiple years, measuring annual change of species distribution would be not practical, but the limitation would be solved in the further studies (e.g, National Ecosystem survey IV) by accumulation of the data from the ongoing national ecosystem survey. Second, the other species which is not incorporated in this study may affect the association. For example, there are several species in insectivore which are in the same trophic hierarchy as rodents could limit the rodent population as competitors. Third, vaccination rate which could be different by regions was not incorporated due to lack of accessibility. However, the vaccination would not be a confounder between the association between species richness and HFRS incidence, because the it cannot have influence on species richness. Fourth, the effect of evenness of wildlife cannot be examined, as the population size data for each species was not possible to obtain however it would have effects on the HFRS incidence as well. Although there has been several field survey in Korea, systematic survey that cover all country with identical methodologies would be needed for ecological study and also public health purpose. Fifth, the study unit, sigungu was used in this study,

would affect the results, in that different scale of study unit (e.g, 1km2 grid) would produce different sample size and values in explanatory variables (Modifiable area unit problem, MAUP).

Nevertheless, the study results had important implication on both public health and wildlife conservation. In the human public health perspectives, the founded association could be applied to predict the risk areas considering the fluctuation of species richness. Moreover, because the increasing predator species richness could be a practical intervention (there is already an activated project), fundamental and pre-emptive countermeasures with ecological point of view would be developed with collaboration with environmental department. This holistic strategy is an example of "One Health approach" which has been advocated by Korean government, recently. Furthermore, the study results support the need of wildlife conservation with utilitarian point of view which may facilitate advocating publics and political changes.

Chapter V.

Overall discussion: Synthesis of results and comments on utilitarian approaches towards wildlife conservation using One Health approach.

5.1. Synthesis of the results

In conclusion, the study results showed that species richness of predators which have same circadian rhythm showed protective effect in chapter 3, 4, but not significant in chapter 2. Species richness of predators which have different circadian rhythm, on the other hands, showed risk effect only in chapter 3, and dilution effect has been shown in chapter 2, 3, whereas the associations were not significant in chapter 4. (Table 5-1).

Table 5-1. Comparison of study results

SR**	Relative risk (95% credible intervals) from Final models*		
	Chapter 2	Chapter 3	Chapter 4
Rodents	**0.909 (0.850 – 0.972)**	**0.906 (0.878 – 0.934)**	1.071 (0.997 – 1.150)
Predators (same circadian rhythm)	1.074 (0.919 – 1.255)	**0.949 (0.907 – 0.993)**	**0.899 (0.826 – 0.975)**
Predators (different circadian rhythm)	1.061 (0.994 – 1.133)	**1.371 (1.258 – 1.499)**	0.995 (0.841 – 1.181)

*Final models: Multivariable analysis including all species richness adjusted by socioeconomic, climate, deforest, land cover, geographic factors (full model)

**Species richness: the number of species

Note: Results of chapter 2 and 3 were obtained from logistic regression in the text. Although the chapter 3 result was odds ratio, that was interpreted as relative risk since its outcome was rare. Meanwhile, Zou's modified Poisson regression model was incorporated to estimate RR in chapter 2, since it had relatively common outcome.

In terms of dilution effects from rodent species richness, both chapter 2 and 3 showed relevant association, supporting that the hypothesis, but in chapter 4 (Korea) the effect did not work. Possibly because the major reservoir rodent in Korea is "super-dominant" which account for 80% of total rodent population in Korea. In other words, the effect of other species may not be functioning, due to relatively small abundance than reservoirs.

The effects of predators of same circadian rhythms with the major reservoir rodents were consistent with the hypothesis in both chapter 3 and 4 (the results showed significant negative association of predator species richness). It implied the regulatory effect of predator species richness, but it was not represented in chapter 2 (West Africa). Considering that the reservoir species in West Africa is nocturnal and non-dominant species (94), and the predation pressure tend to focus on dominant species (95), the predation pressure may not be effective for the reservoir, and rather tend to toward non-reservoir, nocturnal and dominant rodent species in West Africa (regulatory pressure of ② in Figure 5-2)

Only chapter 3 (Brazil) showed significant positive association of predator species richness of different circadian rhythm from reservoir rodents. It was consistent with the hypothesis 1 indirectly, in that the regulatory pressures towards non-diurnal rodents may amplify activities of diurnal rodents which include major rodents in Brazil. However, both chapter 2, 4 did not show significant association. It would be because the effect may need sufficient abundance of rodents which have

different circadian rhythm. For example, diurnal species of rodent in West Africa is outnumbered by nocturnal, and the reservoir rodent is super dominant in Korea, so again, outnumbered the non-diurnal species (regulatory pressure of ③ in Figure 5-1 and Figure 5-3).

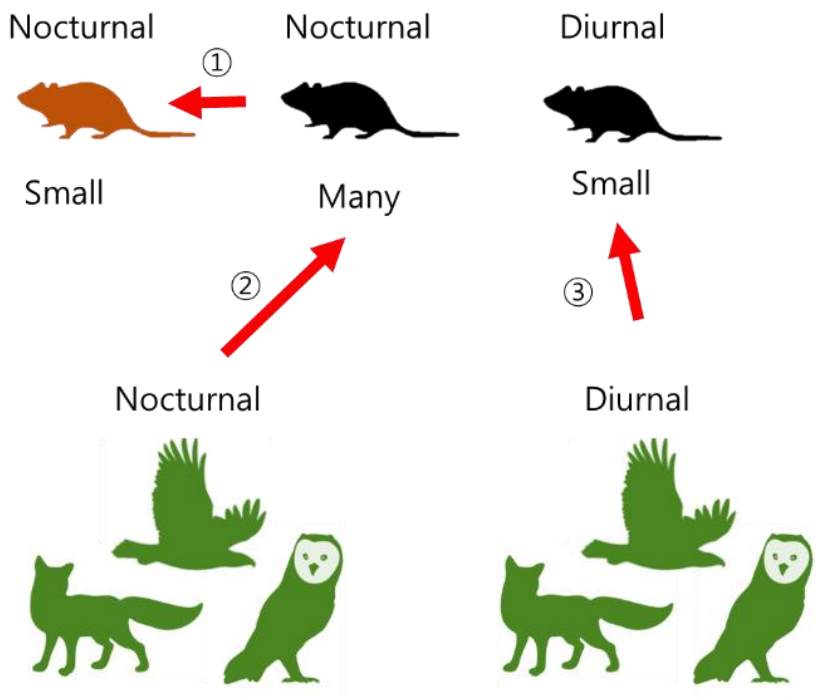

Figure 5-1. Interactions between species in West Africa (chapter 2)

Note: regulatory pressure ① indicates dilution effect that from non-reservoir nocturnal species and diurnal species to nocturnal reservoirs (Major species) in West Africa. Since the non-reservoir nocturnal and diurnal rodents outnumber the nocturnal reservoir in West Africa, the dilution effect would be functioning. Meanwhile, the regulatory pressure of nocturnal predator (②) tend to toward non-reservoir nocturnal rodents and the regulatory pressure of non-nocturnal predator (③) towards diurnal rodents. Therefore, both predators' regulatory pressures were limited to nocturnal reservoir species

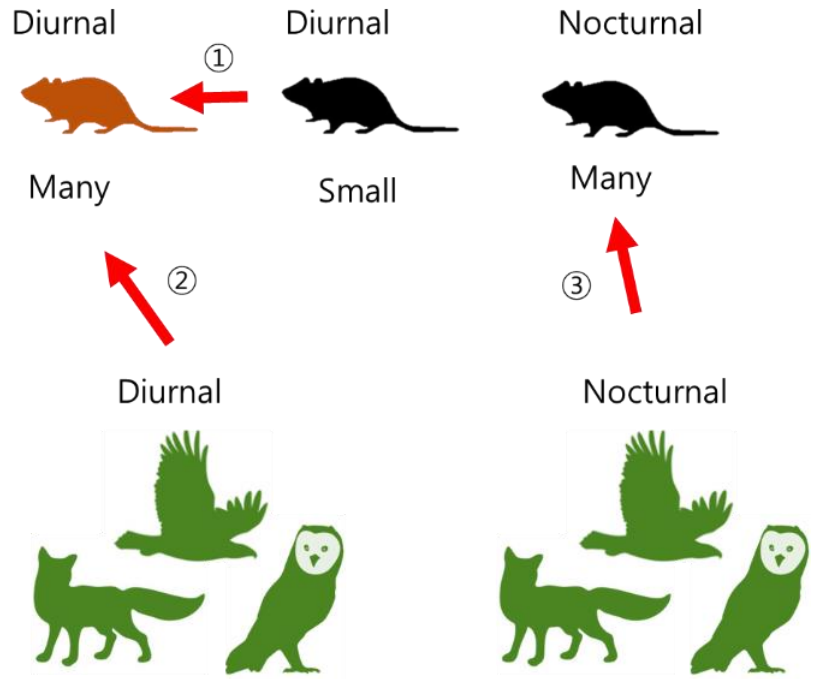

Figure 5-2. Interactions between species in Brazil (chapter 3)

Note: regulatory pressure ① indicates dilution effect that from non-reservoir diurnal species and non-diurnal species to diurnal reservoirs (Major species) in Brazil. Since the non-reservoir diurnal and non-diurnal rodents outnumber the diurnal reservoir in Brazil, the dilution effect would be functioning. Meanwhile, the regulatory pressure of diurnal predator (②) tend to toward reservoir diurnal rodents, so represented protective effect for human hantavirosis. The regulatory pressure of non-diurnal predator (③) towards non-diurnal rodents of which density would be big enough to represent the indirect amplifying effects of the nocturnal predator richness.

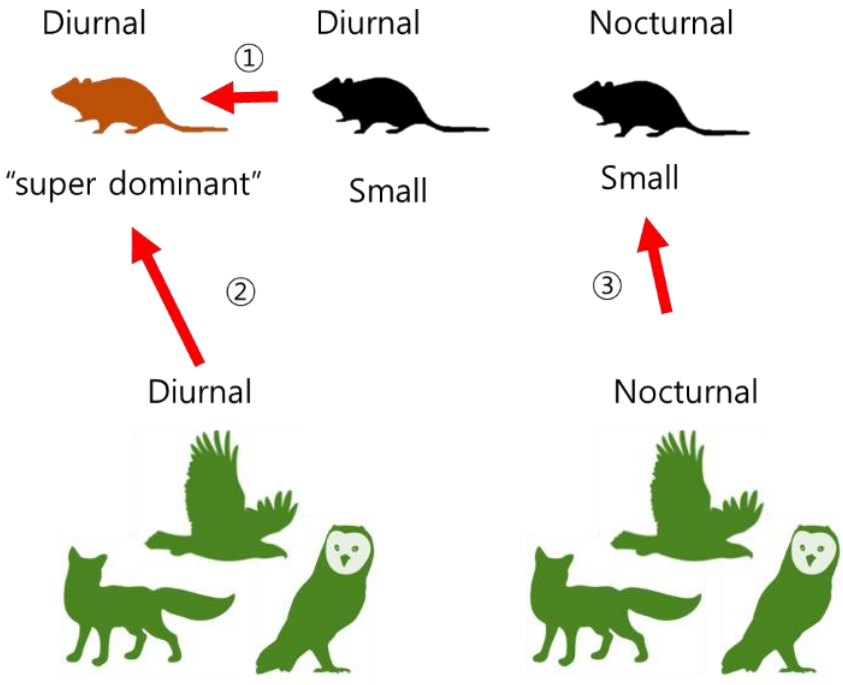

Figure 5-3. Interactions between species in Korea (chapter 4)

Note: regulatory pressure ① indicates dilution effect that from non-reservoir diurnal species and non-diurnal species to diurnal reservoirs (Major species) in Korea. Since the non-reservoir diurnal and non-diurnal rodents were outnumbered by the diurnal reservoir in Korea, the dilution effect would not be functioning. Meanwhile, the regulatory pressure of diurnal predator (②) tend to toward reservoir diurnal rodents, so represented protective effect for human hantavirosis. The regulatory pressure of non-diurnal predator (③) towards non-diurnal rodents of which density would not be big enough to represent the indirect amplifying effects of the nocturnal predator richness.

5.2. Implications on public health

Public health interventions against environmental-borne diseases, including vector-borne diseases and zoonosis, have been relatively ignored the environmental factors, paradoxically. The one of main reason would be that the environmental factors have not been considered as modifiable factors. In comparison with other risk factors, such as outdoor activities, wearing short sleeves, which can be a direct subject of public health intervention, environmental factors, such as temperature, precipitation, land cover, and altitude are impossible to make difference by interventions. In terms of species richness, however, it is practically possible to implement intervention. For example, restoration of Asiatic black bear has been conducted in South Korea from Korea National Park service, and various activities for preventing extinction of species has also been encouraged.

Understanding the association of environmental factors is also important for predict risk area of disease incidence. Even if some explanatory factors were not modifiable, prediction of risk by them would reduce disease burden and facilitate risk communication between health authorities and public. To this end, multidisciplinary approaches is important. In other words, the information on species richness could be easily accessible by public health sectors. So far this holistic approaches have not been widely employed in South Korea, but current direction of inter-government responses on infectious diseases, named as One Health framework, is considered as optimistic

5.3. Implications on wildlife conservation

Previous approaches on wildlife conservation has largely based on Deontological ethics, especially for preservationists, rather than Utilitarianism. For example, one of major strategies that many activists of wildlife conservation employed is appealing to emotion of public by using the aesthetical value of wildlife (e.g. showing an isolated polar bear in an ice floe). Although these tactics could address the issue quickly and aggressively, the following behavioral changes tend to be one-time rather than long-term, and more importantly, institutional-level development is not likely to be realized (The criticism is similar for "poverty porn" in the global health domain).

Utilitarian point of view, in this regards, provides opportunities to increase the effectiveness and impact of wildlife conservation. Emphasizing the close relationship between health of wildlife (diversity is one of indicators) and human health, which could be delivered by various types of research, may facilitate the policy level changes. In this study, I showed the effect of species richness calculated only by species of "Least Concern" (an IUCN category indicating the lowest risk of extinction and showing stable population) in the main analysis, but studies like investigating the effect of extinct or decreasing species as a future studies. Although proving the existence of causal association is not enough to bridge the institutional changes, economic evaluation of intervention toward wildlife conservation including consideration of public health perspective would increase the political drive. The utilitarian approach is not only benefit for the top-down institutional level changes,

but also the bottom-up level behavioral changes of public, since it may persuade them with rational basis which was the weakness of current strategies of wildlife conservation movement.

5.4. Comments on the One Health approaches in South Korea

Since the first One Health forum in 2012, with participation of many researchers from various academic domain in South Korea, there has been a lot of discussions about “One Health”, e.g., the concept and main idea of One Health initiative. Especially in veterinary science, the concept is well-adopted and the relevant discussions have been highly activated. The frequency of use term “One Health” has increased in both academic papers and press journal and surged sometimes, in zoonotic disease outbreak such as MERS and avian influenza.

Not only the use of term, but also practical incorporation of the framework has been observed. Chun et al assessed the PTSD risk of quarantine workers during FMD outbreak in Korea which showed that the effect of animal disease outbreak is not limited to zoonoses. Recently, the Rural development administration initiate the researches on companion animals with a focus on human health.

In contrast, the researches with multi-disciplinary approaches between wildlife sectors and public health sectors have been relatively ignored. Previously the main barriers between two domains were data availability and academic distance. Decades ago, data collection was conducted individually in both sectors, which was seldom national level, making difficult to share. But recent surge of the national level data which are usually open access provides optimistic opportunities to collaborate the two heterogeneous field. Although still there is a long way to go, the collaboration will benefit for both of disciplines

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Acronyms

AIC Akaike information criterion

GFC Global Forest Change

GIDEON Global Infectious Disease and Epidemiology Network

HFRS hemorrhagic fever with renal syndrome

HPS hantavirus pulmonary syndrome

IUCN International Union for Conservation of Nature

KCDC Korean Center for Disease Control and Prevention

KOSIS Korean Statistical Information Service

MRU Mano River union

RBD rodent-borne disease

VBD vector-borne disease

WHO DON World Health Organization Disease Outbreak News

Supplementary materials

Appendix 1-1. Scoping review process

1. Framework

1.1. Key references

In this scoping review, I referred to Center for Reviews and Dissemination (CRD)'s guidance for undertaking reviews in health care and NECA manual for systematic review (Korean)

1.2. Database

To select database for the Scoping review, I followed COSI model, as US National Library of Medicine suggested. Specifically, I used Medline and Embase which are categorized as core database in the model.

2. Search term selection

2.1. Term selection framework

To select search terms, I followed the PICO framework, but I used terms only related to Problems (P) AND predictors (I) to maximize sensitivity of the literature review

2.2. Problems (VBDs)

2.2.1. Disease lists

Category 1	Category 2	Mesh term	Emtree
General term	Mosquito borne		
	Tick-borne	Tick-borne diseases	Tick borne disease
	Mite-borne		
	Rodent-borne		
	arbovirus	arbovirus infections, arboviruses	arbovirus
	Vector-borne diseases		
Mosquito-borne	Malaria	Malaria	malaria
	Dengue	Dengue	Dengue
	Lymphatic filariasis	Elephantiasis, filarial	lymphatic filariasis
	Chikungunya	Chikungunya fever, Chikungunya virus	
	Zika	Zika virus infection, Zika virus	
	Yellow fever	Yellow fever, Yellow fever virus	
	Japanese encephalitis	Encephalitis, japanese, encephalitis viruses, japanese, encephalitis virus, japanese	
	Westnile	West nile fever, West nile virus	
	Rift Valley fever	Rift valley fever, Rift valley fever virus	

Tick-borne	Relapsing fever	Relapsing fever	Borrelia infection
(Mite-borne)	lyme disease	Lyme disease, lyme neuroborreliosis	Lyme disease
	Tick-borne encephalitis	Encephalitis, tick-borne, encephalitis viruses, tick-borne	
	Tularemia	Tularemia	Tularemia
	Spotted fever	Rocky mountain spotted fever	Rocky mountain spotted fever
	Crimean-congo haemorrhagic fever	Hemorrhagic fever, Crimean	Crimean-congo haemorrhagic fever, Crimean-congo haemorrhagic fever virus
	Scrub typhus*	Scrub typhus	Scrub typhus
	SFTS*	Phlebovirus	`Phlebovirus infection
Rodent-borne	hantavirus pulmonary syndrome	hantavirus, hantavirus infection, hantavirus pulmonary syndrome	
	Hemorrhagic fever with renal syndrome	Hemorrhagic fever with renal syndrome	Hemorrhagic fever with renal syndrome
	Lassa fever	Lassa fever	Lassa fever
	Leptospirosis	leptospirosis	leptospirosis
	Lymphocytic chorio-meningitis (LCM)	Lymphocytic choriomeningitis, Lymphocytic choriomeningitis virus	Lymphocytic choriomeningitis virus
	Omsk hemorrhagic fever	Hemorrhagic fever, Omsk	
	Plague	plague	plague
	Rat-bite fever	Rat-bite fever	rat bite fever
	South American Arenaviruses	Arenaviruses, New world	New world arenavirus

Others	Leishmaniasis	Leishmaniasis, Leishmaniasis, Cutaneous, Leishmaniasis, Visceral	Leishmaniasis, skin leishmaniasis, visceral leishmaniasis
	Sandfly fever	Phlebotomus fever, Sandfly fever Naples virus	Sandfly fever, phlebovirus
	Chagas	Chagas disease, Chagas cardiomyopathy	Chagas disease, Chagas cardiomyopathy
	Sleeping sickness	Trypanosomiasis, African	African trypanosomiasis
	Onchocerciasis	Onchocerciasis	Onchocerciasis
	Schistosomiasis	Schistosomiasis	Schistosomiasis
	Zoonosis***	zoonoses	zoonosis
	Neglectd tropical diseases***	neglected diseases	neglected disease
	Emerging infectious diseases***	Communicable diseases, emerging	disease re-emergence
	Pathogen		

* Not listed in the references but added due to endemicity in Korea

** Google search, wikipedia, WHO, CDC

*** Many diseases in the categories are Vector-borne

2.2.2. Vectors

Category 1	Category 2	Mesh term	Emtree
General term	Vectors	arthropod vector	arthropod vector
	Mosquitoes	Mosquito vectors	mosquito vector
	Flies	Diptera, Tephritidae, Muscidae	Diptera, Tephritidae, Muscidae
	Ticks	Ornithodoros	Tick, Ornithodoros
	Mites	Mites	Mite
	Rodents	Rodentia	rodent
Mosquitoes	Aedes	Aedes	Aedes, Aedes aegypti, Aedes albopictus
	Anopheles	Anopheles	Anopheles
	Culex	Culex	Culex
Flies	Sandflies	Psychodidae	Phlebotominae
	Tsetse flies	Tsetse flies	Glossinidae
	Black flies	Simuliidae	Simuliidae
Others	Triatomine bugs	Triatominae	Triatominae
	Fleas	Siphonaptera	Flea
	Aquatic snails	Biomphalaria	Biomphalaria

2.3. Main exposure (Predictors)

2.3.1. Search term list

Category 1	Category 2	Mesh term	Emtree
General term	Preservation		
	Conservation	Conservation of natural resources	
	Forest	forests, rainforest	forest
Effects/Therories	Dilution effect		
	amplification effect		
	Spillover		
Deforestation	Deforestation		deforestation
	forest loss		
	forest cover		
	land cover		land use
	forest destruction		
	logging		
	fragmentation		
Biodiversity	Biodiversity	Biodiversity	biodiversity
	Species richness		Species richness
	species abundance		population abundance
	biotic homogenization		
	extinction	Extinction, biological	
	endangered species	Endangered species	
Species*	mammals	mammals	mammal
	birds	Birds	bird
	amphibians	amphibians	amphibia
	reptiles	Reptiles	reptile

* IUCN provided global distribution of species for mammals, birds, amphibians, and reptiles, subsequently majority of relevant studies include these species in their models

3. Search terms

Category 1	Category 2	#	Search term for PUBMED
General term	Mosquito borne	1	"Mosquito-borne disease" OR "Mosquito-borne illness" OR "Mosquito-borne tropical disease" OR "Mosquito-borne infectious disease" OR "Mosquito-borne diseases" OR "Mosquito-borne tropical diseases" OR "Mosquito-borne infectious diseases"
	Tick borne	2	"Tick-borne diseases"[Mesh] OR tibovirus
	Mite borne	3	"Mite-borne diseases" OR "Mite-borne illness" OR "Mite-borne disease"
	Rodent-borne	4	"Rodent-borne diseases" OR "Rodent-borne illness" OR "Rodent-borne disease"
	arbovirus	5	"arbovirus infections"[Mesh] OR arboviruses[Mesh] OR "arthropod-borne disease" OR "arthropod-borne illness" OR "arthropod-borne diseases"
	Vector-borne diseases	6	"Vector-borne disease" OR "Vector-borne illness" OR "Vector-borne diseases"
	Zoonosis	7	Zoonoses[Mesh] OR Zoonosis OR "Zoonotic diseases" OR "Zoonotic disease"
	Neglected tropical diseases	8	"Neglected diseases"[Mesh] OR "Neglected tropical diseases" OR "Neglected zoonotic diseases" OR "Tropical diseases" OR "Neglected tropical disease" OR "Neglected zoonotic disease" OR "Tropical disease"
	Emerging infectious diseases	9	"Communicable diseases, emerging"[Mesh] OR "emerging infectious diseases" OR "newly emerging infectious diseases" OR "re-emerging infectious diseases" OR "emerging infectious disease" OR "newly emerging infectious disease" OR "re-emerging infectious disease"
Mosquito-borne	Malaria	10	Malaria[Mesh] OR Plasmodium
	Dengue	11	Dengue[Mesh] OR "Dengue fever" OR "dengue hemorrhagic fever" OR "dengue shock syndrome"
	Lymphatic filariasis	12	"Elephantiasis, filarial"[Mesh] OR Elephantiasis OR "Wuchereria bancrofti" OR "brugia malayi" OR "brugia timori"
	Chikungunya	13	"Chikungunya fever"[Mesh] OR "Chikungunya virus"[Mesh]

	Zika	14	"Zika virus infection"[Mesh] OR "Zika virus"[Mesh]
	Yellow fever	15	"Yellow fever"[Mesh] OR "Yellow fever virus"[Mesh]
	Japanese encephalitis	16	"Encephalitis, japanese"[Mesh] OR "Encephalitis viruses, japanese"[Mesh] OR "Encephalitis virus, japanese"[Mesh]
	West nile	17	"West nile fever"[Mesh] OR "West nile virus"[Mesh]
	Rift valley fever	18	"Rift valley fever"[Mesh] OR "Rift valley fever virus"[Mesh]
Tick-borne, Mite-borne	Relapsing fever	19	"Relapsing fever"[Mesh] OR "Tick-borne relapsing fever" OR "relapsing fever borreliosis" OR "Louse-borne relapsing fever"
	lyme disease	20	"Lyme disease"[Mesh] OR "Lyme neuroborreliosis"[Mesh] OR "Borrelia burgdorferi" OR "lyme borreliosis"
	Tick-borne encephalitis	21	"Encephalitis, tick-borne"[Mesh] OR "encephalitis viruses, tick-borne"[Mesh]
	Tularemia	22	Tularemia[Mesh] OR "Francisella tularensis"
	Spotted fever	23	"Rocky mountain spotted fever"[Mesh] OR "Mediterranean spotted fever" OR "Queensland tick typhus" OR "helvetica spotted fever"
	Crimean-congo haemorrhagic fever	24	"Hemorrhagic fever, Crimean"[Mesh] OR "Hemorrhagic fever virus" OR "crimean-congo"
	Scrub typhus	25	"Scrub typhus"[Mesh] OR Tsutsugamushi OR "bush typhus" OR Orientia
	SFTS	26	Phlebovirus[Mesh] OR SFTS OR "severe fever with thrombocytopenia syndrome"
Rodent-borne	Hantavirus pulmonary syndrome	27	hantavirus[Mesh] OR "hantavirus infection"[Mesh] OR "hantavirus pulmonary syndrome"[Mesh]
	hemorrhagic fever with renal syndrome	28	"Hemorrhagic fever with renal syndrome"[Mesh] OR "hantaan virus" OR "seoul virus"

	lassa fever	29	"Lassa fever"[Mesh] OR "Lassa hemorrhagic fever"
	leptospirosis	30	leptospirosis[Mesh] OR "Weil Disease"
	Lymphocytic chorio-meningitis (LCM)	31	"Lymphocytic choriomeningitis"[Mesh] OR "Lymphocytic choriomeningitis virus"[Mesh] OR "Lymphocytic choriomeningitis" OR "Benign lymphocytic meningitis" OR "Lymphocytic meningoencephalitis" OR "Serous lymphocytic meningitis"
	Omsk hemorrhagic fever	32	"Hemorrhagic fever, Omsk"[Mesh]
	Plague	33	Plague[Mesh] OR "Yesinia pestis" OR "bubonic plague" OR "septicemic plague" OR "pneumonic plague" OR "Meningeal plague"
	Rat-bite fever	34	"Rat-bite fever"[Mesh] OR sodoku
	South American Arenaviruses	35	"Arenaviruses, New world"[Mesh] OR "Argentine hemorrhagic fever" OR "Bolivian hemorrhagic fever" OR "Bolivian hemorrhagic fever" OR "Venezuelan hemorrhagic fever"
Others	Leishmaniasis	36	Leishmaniasis[Mesh] OR "Leishmaniasis, Cutaneous"[Mesh] OR "Leishmaniasis, Visceral"[Mesh] OR "mucocutaneous leishmaniasis" OR "black fever" OR "kala-azar"
	Sandfly fever	37	"Phlebotomus fever"[Mesh] OR "Sandfly fever"[Mesh] OR "Naples virus"[Mesh]
	Chagas	38	"Chagas disease"[Mesh] OR "Chagas cardiomyopathy"[Mesh] OR "American trypanosomiasis" OR "trypanosoma cruzi"
	Sleeping sickness	39	"Trypanosomiasis, African"[Mesh] OR "sleeping sickness" OR "trypanosoma brucei"
	Onchocerciasis	40	Onchocerciasis[Mesh] OR "river blindness" OR "robles diseases"
	Schistosomiasis	41	Schistosomiasis[Mesh] OR Bilharziasis OR "snail fever"
General term	Vectors	42	"Arthropod vector"[Mesh] OR vectors OR vector OR "disease vector" OR "disease vectors"
	Mosqutioes	43	"Mosquito vectors"[Mesh] OR Culicidae OR Mosquito OR "Mosquito-bite"

	Flies	44	Diptera[Mesh] OR Tephritidae[Mesh] OR Muscidae[Mesh] OR fly OR flies OR "blood-sucking fly" OR "blood-sucking flies" OR "biting flies" OR "biting fly"
	Ticks	45	Ornithodoros[Mesh] OR "tick-bite" OR ticks OR tick
	Mites	46	Mites[Mesh] OR Trombiculidae OR Acaridae OR Pyroglyphidae
	Rodents	47	Rodentia[Mesh] OR rat OR mouse OR mice OR murine
Mosquitoes	Aedes	48	Aedes[Mesh] OR "Aedes aegypti" OR "Aedes albopictus"
	Anopheles	49	Anopheles[Mesh]
	Culex	50	Culex[Mesh]
Flies	Sandflies	51	Psychodidae[Mesh] OR Sandflies OR Sandfly
	Tsetse flies	52	"Tsetse flies"[Mesh] OR Glossinidae
	Black flies	53	Simuliidae[Mesh] OR "black flies" OR "black fly"
Others	Triatomine bugs	54	Triatominae[Mesh] OR "Triatomine bugs"
	Fleas	55	Siphonaptera[Mesh] OR fleas OR flea
	Aquatic snails	56	Biomphalaria[Mesh] OR "freshwater snails" OR "Aquatic snails"
General term	Preservation	57	Preservation OR "Environmental preservation" OR "forest preservation"
	Conservation	58	"Conservation of natural resources"[Mesh] OR conservation OR "Environmental conservation" OR "forest conservation"
	Forest	59	forests[Mesh] OR rainforest[Mesh]
Deforestation	Deforestation	60	Deforestation OR "Forest loss" OR "Forest destruction" OR logging OR fragmentation
	forest cover	61	"forest cover" OR "land cover" OR "land use"
Biodiversity	biodiversity	62	biodiversity[Mesh] OR "Species richness" OR "Species abundance" OR "biotic homogenization"
	extinction	63	"Extinction, biological"[Mesh] OR extinction OR "Endangered species"[Mesh]

Effects/Theories	Dilution effect	64	"Dilution effect"
	amplification effect	65	"Amplification effect"
	spillover	66	Spillover
Species	Mammals	67	Mammals[Mesh]
	Avians	68	Birds[Mesh]
	Amphibians	69	Amphibians[Mesh]
	Reptiles	70	Reptiles[Mesh]
other than original		71	review[pt] OR editorial[pt] OR case reports[pt] letter[pt] OR newspaper article[pt] OR comment[pt]
review		72	review[pt]
		73	English[lang]

Appendix 2-1. Lassa fever outbreak data synthesis

Table S2-1. The list of Lassa fever outbreak regions

ID	Country	region	Category
1	Benin	Atakora Department	
2	Benin	Atlantique	
3	Benin	Alibori	
4	Benin	Borgou Department	
5	Benin	Collines	
6	Benin	Donga Department	
7	Benin	Oueme Department	
8	Benin	Plateau	
9	Ghana	Ashanti	
10	Ghana	Eastern Region	
11	Liberia	Bong County	Before 2006
12	Liberia	Bomi county	Before 2006
13	Liberia	Grand Bassa	
14	Liberia	Lofa County	Before 2006
15	Liberia	Nimba County	Before 2006
16	liberia	Margibi (county)	
17	liberia	Montserrado County	Before 2006
18	Mali	Sikasso region	
19	Mali	Segou region	Before 2006
20	Nigeria	Adamawa State	Before 2006
21	Nigeria	Akwa Iborn State	
22	Nigeria	Anambra State	
23	Nigeria	Bauchi State	
24	Nigeria	Benue	Before 2006
25	Nigeria	Borno	Before 2006
26	Nigeria	Cross-River	
27	Nigeria	Delta State	
28	Nigeria	East Central State	Before 2006
29	Nigeria	Ebonyi State	

30	Nigeria	Edo State	Before 2006
31	Nigeria	Ekiti State	
32	Nigeria	Enugu	
33	Nigeria	Federal Capital Territory	
34	Nigeria	Gombe State	
35	Nigeria	Imo State	Before 2006
36	Nigeria	Kaduna State	Before 2006
37	Nigeria	Katsina	
38	Nigeria	Kebbi	
39	Nigeria	Kano State	
40	Nigeria	Kogi State	
41	Nigeria	Kwara	
42	Nigeria	Lagos State	
43	Nigeria	Nasarawa State	
44	Nigeria	Ogun State	
45	Nigeria	Ondo State	
46	Nigeria	Osun State	
47	Nigeria	Oyo State	
48	Nigeria	Plateau State	Before 2006
49	Nigeria	Rivers State	
50	Nigeria	Sokoto	Before 2006
51	Nigeria	Taraba	
52	Nigeria	Yobe	
53	Sierra Leone	Kailahun District, eastern	Before 2006
54	Sierra Leone	Tonkolili, northern	
55	Sierra Leone	Wester Area Rural,western	
56	Sierra Leone	Bo,southern	Before 2006
57	Sierra Leone	Makeni (village), northern	
58	Sierra Leone	Kameni (town)	
59	Sierra Leone	Kenema, eastern	Before 2006
60	Sierra Leone	Kono District, eastern	Before 2006
61	Sierra Leone	Pujehun District, southern	Before 2006
62	Sierra Leone	Moyamba District, southern	Before 2006

63	Sierra Leone	Paguma (Eastern)	Before 2006
64	Sierra Leone	South & East	Before 2006
65	Sierra Leone	free town,western	Before 2006
66	Togo	Oti (district), Savanes	
67	Togo	Kpendjal (district) Savanes	
68	Burkina Faso	Ouargaye (district)	
69	Burkina Faso	Como?Province	Before 2006
70	Cote d'Ivoire	Beoumi Prefecture	Before 2006
71	Guinea	Faranah Prefecture	Before 2006
72	Guinea	Kindia Prefecture	Before 2006
73	Guinea	Kissidougou Prefecture	Before 2006
74	Guinea	Macenta Prefecture	Before 2006
75	Guinea	Nz??or?Prefecture	Before 2006
76	Ginea	Pita	Before 2006
77	Ginea	Gueckedou	Before 2006

Appendix 2-2. Species included to count species richness in Western Africa

Table S2-2. carnivore species included

Academic names	Common names	Korean names	IUCN	Behavior
Vulpes pallida	pale fox	검은꼬리모래 여우	LC	Nocturnal
Herpestes ichneumon	Egyptian mongoose	이집트 몽구스	LC	Diurnal
Herpestes naso	Long-nosed mongoose	긴코 몽구스	LC	Diurnal
Mellivora capensis	Honey badger	벌꿀오소리(라텔)	LC	Nocturnal
Genetta johnstoni	johnston's genet	존스턴제넷	NT	Nocturnal
Nandinia binotata	African palm civet	아프리카 팜 사향고양이	LC	Nocturnal
Atilax paludinosus	water mongoose	늪몽구스	LC	Nocturnal
Crossarchus obscurus	cusimanse	쿠시만스	LC	Diurnal
Crossarchus platycephalus	flat-headed cusimanse	납작머리 쿠시만스	LC	Diurnal
Vulpes zerda	fennec fox	페넥여우	LC	Nocturnal
Bdeogale nigripes	black-legged mongoose	검은발몽구스	LC	Nocturnal
Ichneumia albicauda	white-tailed mongoose	흰꼬리몽구스	LC	Nocturnal
Mungos mungo	banded mongoose	줄무늬몽구스	LC	Diurnal
Ictonyx libycus	Saharan striped polecat	사하라줄무늬족제비	LC	Nocturnal

Ictonyx striatus	striped polecat	줄무늬족제비	LC	Nocturnal
Civettictis civetta	African civet	아프리카 사향고양이	LC	Nocturnal
Genetta genetta	common genet	커먼제넷	LC	Nocturnal
Genetta maculata	rusty-spotted genet	붉은점박이제넷	LC	Nocturnal
Poiana richardsonii	african linsang	아프리카린상	LC	Nocturnal
Genetta servalina	servaline genet	서발린제넷	LC	Nocturnal
Genetta thierryi	haussa genet	하우사제넷	LC	Nocturnal
Poiana leightoni	Leighton's linsang	라이톤린상	VU	Nocturnal
Genetta poensis	king genet	왕제넷	DD	Nocturnal
Genetta pardina	west african large spotted genet	서아프리카 큰점박이제넷	LC	Nocturnal
Genetta bourloni	bourlon's genet	부흘롱제넷	VU	Nocturnal
Felis margarita	sand cat	모래고양이	LC	Nocturnal
Felis silvestris	wild cat	들고양이	LC	Nocturnal
Vulpes rueppellii	ruppell's fox	흰꼬리모래여우	LC	Nocturnal
Canis aureus	golden jackal	황금자칼	LC	Nocturnal
Canis adustus	side-striped jackal	가로줄무늬자칼	LC	Nocturnal
Leptailurus serval	serval	서벌	LC	Nocturnal
Caracal caracal	caracal	카라칼	LC	Nocturnal
Genetta cristata	crested servaline genet	볏서발린제넷	VU	Crepuscular

Liberiictis kuhni	liberian mongoose	라이베리아 몽구스	VU	Diurnal
Herpestes sanguineus	slender mongoose	날씬몽구스	LC	Diurnal
Lycaon pictus	african wild dog	아프리카 들개	EN	Crepuscular
Mungos gambianus	gambian mongoose	감비아 몽구스	LC	Diurnal
Caracal aurata	african golden cat	아프리카 황금고양이	VU	Nocturnal

Table S2-3. Carnivore species excluded

Academic names	Common names	Korean names	Exclusion criteria		
			Aquatic prey	Large prey	Scavenger
Aonyx capensis	african clawless otter	아프리카민발톱수달	O		
Aonyx congicus	cameroon clawless otter	카메룬민발톱수달	O		
Hydrictis maculicollis	spotted-necked otter	얼룩목수달	O		
Acinonyx jubatus	cheetah	치타		O	
Hyaena hyaena	striped hyaena	줄무늬하이에나		O	O
Panthera pardus	leopard	표범		O	
Panthera leo	lion	사자		O	
Crocuta crocuta	spotted hyena	점박이하이에나		O	O

Table S2-4. Avian species included

Family name	Academic names	Common names	IUCN	Behavior
Accipitridae	*Accipiter ovampensis*	Ovambo sparrowhawk	LC	Diurnal
Accipitridae	*Buteo auguralis*	red-necked buzzard	LC	Diurnal
Accipitridae	*Micronisus gabar*	garbar goshawk	LC	Diurnal
Accipitridae	*Melierax metabates*	dark chanting goshawk	LC	Diurnal
Accipitridae	*Terathopius ecaudatus*	bateleur	NT	Diurnal
Accipitridae	*Aquila rapax*	tawny eagle	LC	Diurnal
Accipitridae	*Aquila spilogaster*	African hawk eagle	LC	Diurnal
Accipitridae	*Lophaetus occipitalis*	long-crested eagle	LC	Diurnal
Accipitridae	*Kaupifalco monogrammicus*	lizard buzzard	LC	Diurnal
Accipitridae	*Gypohierax angolensis*	palm-nut vulture	LC	Diurnal
Accipitridae	*Milvus migrans*	black kite	LC	Diurnal
Accipitridae	*Chelictinia riocourii*	scissor-tailed kite	LC	Diurnal
Accipitridae	*Hieraaetus ayresii*	Ayres's Hawk-eagle	LC	Diurnal
Accipitridae	*Circaetus beaudouini*	Beaudouin's Snake-eagle	VU	Diurnal
Accipitridae	*Hieraaetus wahlbergi*	Wahlberg's Eagle	LC	Diurnal
Accipitridae	*Accipiter toussenelii*	Red-chested Goshawk	LC	Diurnal
Accipitridae	*Accipiter badius*	Shikra	LC	Diurnal
Accipitridae	*Polyboroides typus*	African Harrier-hawk	LC	Diurnal

Accipitridae	*Accipiter castanilius*	Chestnut-flanked Sparrowhawk	LC	Diurnal
Accipitridae	*Dryotriorchis spectabilis*	Congo Serpent-eagle	LC	Diurnal
Accipitridae	*Polemaetus bellicosus*	Martial Eagle	VU	Diurnal
Accipitridae	*Urotriorchis macrourus*	Long-tailed Hawk	LC	Diurnal
Accipitridae	*Elanus caeruleus*	Black-winged Kite	LC	Diurnal
Accipitridae	*Accipiter erythropus*	Red-legged Sparrowhawk	LC	Diurnal
Accipitridae	*Circaetus cinerascens*	Western Banded Snake-eagle	LC	Diurnal
Accipitridae	*Circaetus cinereus*	Brown Snake-eagle	LC	Diurnal
Accipitridae	*Aviceda cuculoides*	African Cuckoo-hawk	LC	Diurnal
Accipitridae	*Stephanoaetus coronatus*	Crowned Eagle	NT	Diurnal
Accipitridae	*Macheiramphus alcinus*	Bat Hawk	LC	Diurnal
Accipitridae	*Aquila africana*	Cassin's Hawk-eagle	LC	Diurnal
Accipitridae	*Accipiter melanoleucus*	Black Sparrowhawk	LC	Diurnal
Falconidae	*Falco alopex*	Fox Kestrel	LC	Diurnal
Falconidae	*Falco ruficollis*	Red-necked Falcon	LC	Diurnal
Falconidae	*Falco cuvierii*	African Hobby	LC	Diurnal
Falconidae	*Falco ardosiaceus*	Grey Kestrel	LC	Diurnal
Falconidae	*Falco peregrinus*	Peregrine Falcon	LC	Diurnal
Falconidae	*Falco tinnunculus*	Common Kestrel	LC	Diurnal
Falconidae	*Falco biarmicus*	Lanner Falcon	LC	Diurnal
Strigidae	*Ptilopsis leucotis*	Northern White-faced Owl	LC	Nocturnal

Strigidae	*Jubula lettii*	Maned Owl	DD	Nocturnal
Strigidae	*Strix woodfordii*	African Wood Owl	LC	Nocturnal
Strigidae	*Otus icterorhynchus*	Northern White-faced Owl	LC	Nocturnal
Strigidae	*Glaucidium capense*	African Barred Owlet	LC	Nocturnal
Strigidae	*Asio capensis*	Marsh Owl	LC	Nocturnal
Strigidae	*Otus senegalensis*	African Scops-owl	LC	Nocturnal
Strigidae	*Glaucidium perlatum*	Pearl-spotted Owlet	LC	Nocturnal
Strigidae	*Bubo poensis*	Fraser's Eagle-owl	LC	Nocturnal
Strigidae	*Glaucidium sjostedti*	Sjostedt's Owlet	LC	Nocturnal
Strigidae	*Glaucidium tephronotum*	Red-chested Owlet	LC	Nocturnal
Strigidae	*Bubo ascalaphus*	Pharaoh Eagle-owl	LC	Nocturnal
Strigidae	*Bubo cinerascens*	Greyish Eagle-owl	LC	Nocturnal
Strigidae	*Bubo lacteus*	Verreaux's Eagle-owl	LC	Nocturnal
Strigidae	*Bubo leucostictus*	Akun Eagle-owl	LC	Nocturnal
Strigidae	*Bubo shelleyi*	Shelley's Eagle-owl	NT	Nocturnal

Table S2-6. Avian species excluded

Family name	Academic names	Common names	Exclusion criteria	
			Scavenger	Aquatic prey
Accipitridae	*Haliaeetus vocifer*	Black-and-white awkeagle		O
Accipitridae	*Gyps africanus*	White-backed Vulture	O	
Accipitridae	*Gyps rueppelli*	R?ppell's Vulture	O	
Accipitridae	*Necrosyrtes monachus*	Hooded Vulture	O	
Accipitridae	*Neophron percnopterus*	Egyptian Vulture	O	
Accipitridae	*Torgos tracheliotos*	Lappet-faced Vulture	O	
Accipitridae	*Trigonoceps occipitalis*	White-headed Vulture	O	
Strigidae	*Scotopelia bouvieri*	Vermiculated Fishing-owl		O
Strigidae	*Scotopelia peli*	Pel's Fishing-owl		O
Strigidae	*Scotopelia ussheri*	Rufous Fishing-owl		O

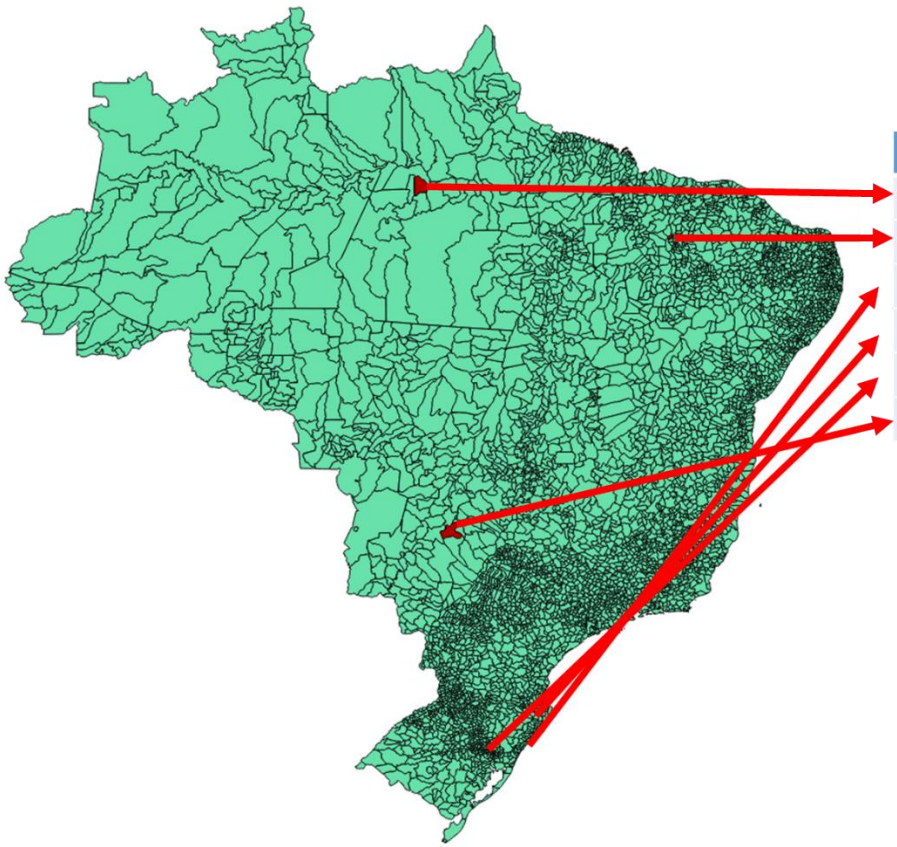
Appendix 3-1. Standardization of Brazil administrative region

Step 1. Figure out the number of municipality changes in Brazil

Table S3-1. Changes of number of municipalities in brazil

Year	Municipalities
1994	4974
2000	5507
2003	5560
2004	5560
2005	5564
2006	5564
2007	5564
2008	5564
2009	5565
2010	5565
2011	5565
2012	5565
2013	5570
2014	5570

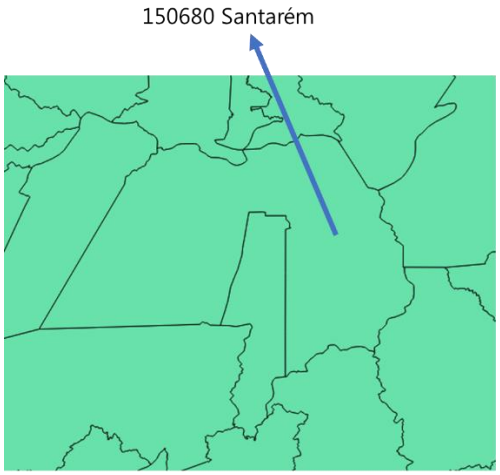
Step 2. Identify the newly added municipalities

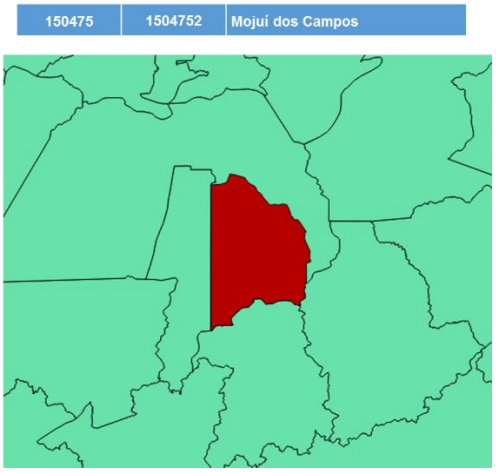


New municipality

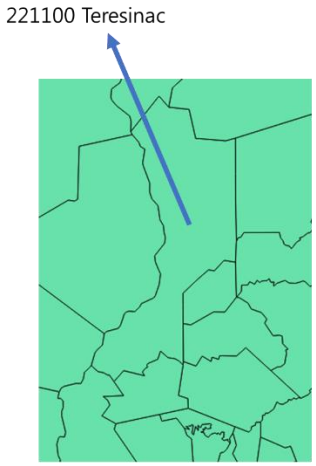
ID	6 digit ID	Name of municipalities
1	150475	Mojuí dos Campos
2	220672	Nazária
3	422000	Balneário Rincão
4	421265	Pescaria Brava
5	431454	Pinto Bandeira
6	500627	Paraíso das Águas

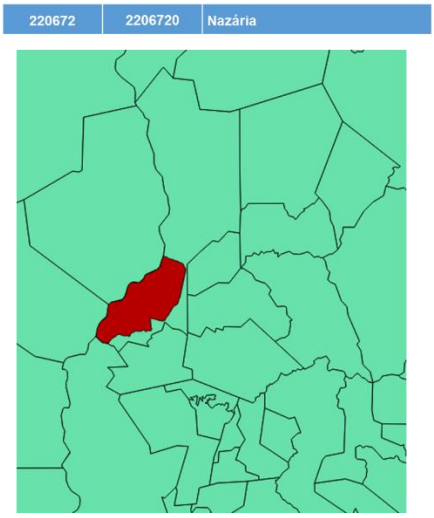
#1 Santarem



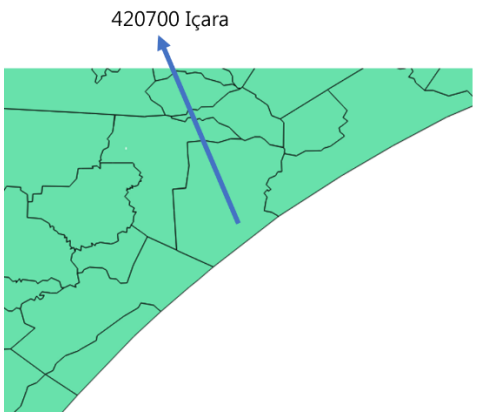


#2 Teresinac

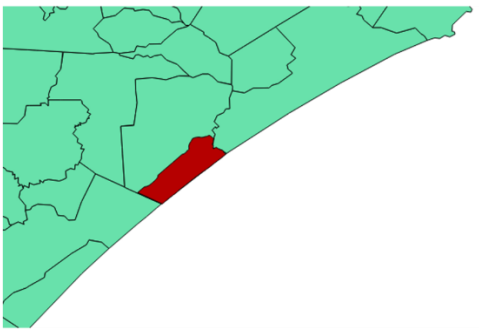




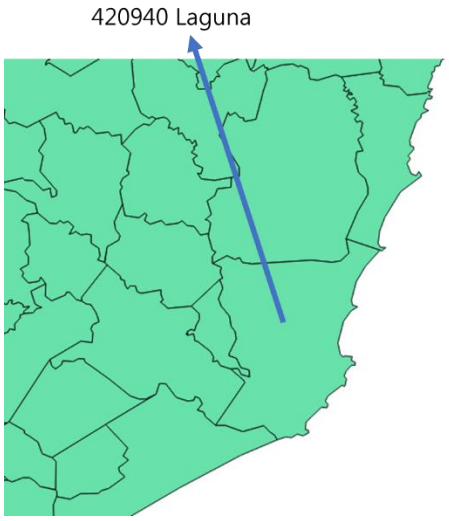
#3 Icara



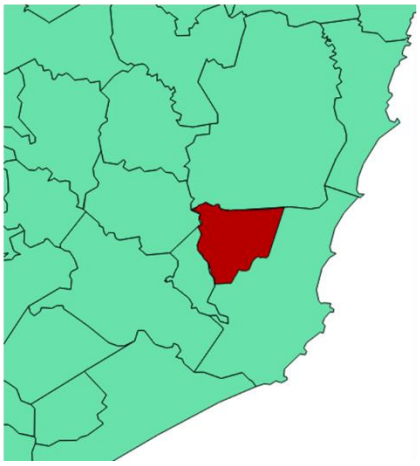
422000	4220000	Balneário Rincão



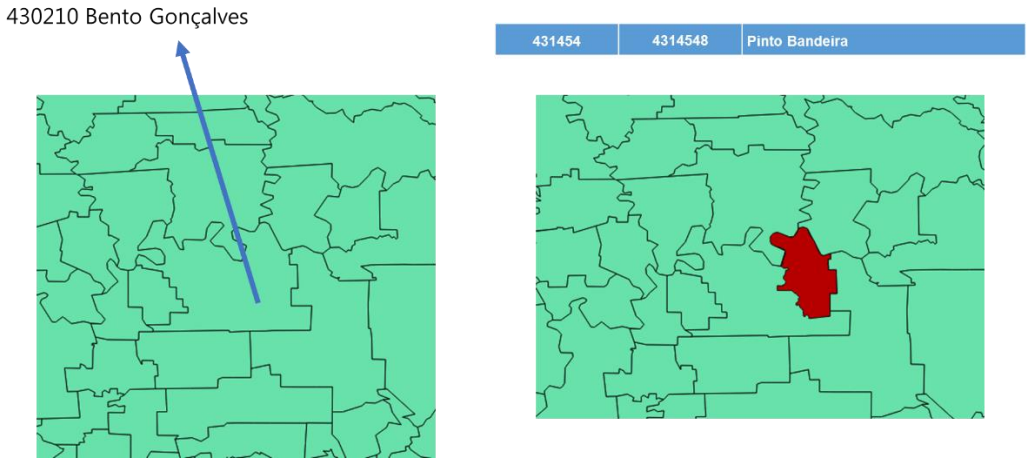
#4 Laguna



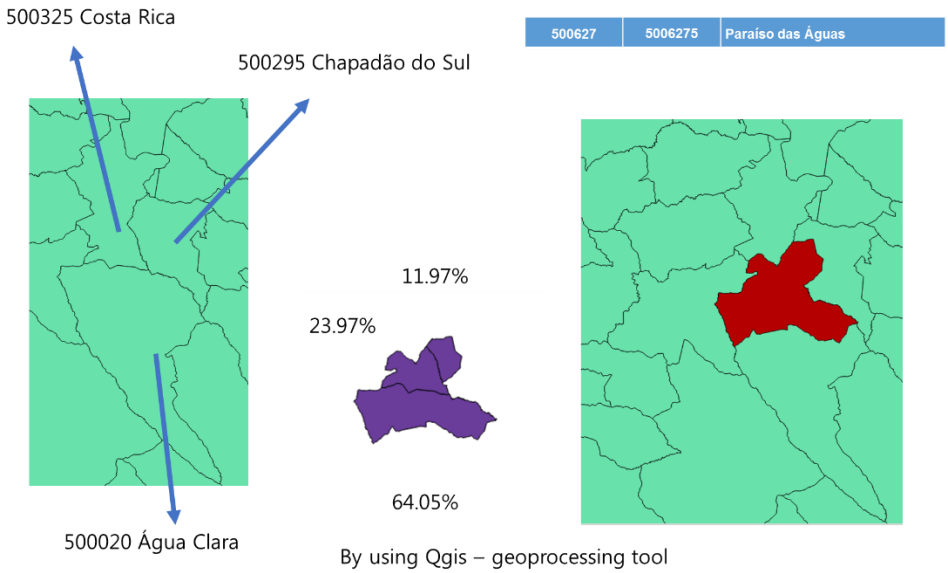
421265	4212650	Pescaria Brava



#5. Bento Goncalves



#6 Costa Rica, Chapadao do sul, Agua Clara



By using Qgis – geoprocessing tool

Appendix 3-2. Species included to count species richness in Brazil

Table S3-2. carnivore species included

academic	common	korean	IUCN	Behavior
Cerdocyon thous	common zorro	게잡이 여우	LC	Nocturnal
Chrysocyon brachyurus	maned wolf	갈기늑대	NT	Nocturnal
Atelocynus microtis	short-eared dog	작은귀개	NT	Diurnal
Lycalopex vetulus	hoary fox	호리여우, 회백색여우	LC	Nocturnal
Lycalopex gymnocercus	pampas fox	팜파스 여우	LC	Nocturnal
Herpailurus yagouaroundi	jaguarundi	재규어런디	LC	Diurnal
Leopardus pardalis	ocelot	오셀롯	LC	CATHEMERAL
Leopardus wiedii	Magay	마게이	NT	Nocturnal
Mustela africana	Amazon weasel	아마존 족제비	LC	Diurnal
Leopardus colocolo	pampas cat	콜로콜로	NT	Nocturnal
Leopardus geoffroyi	Geofforoy's cat	조프루아고양이	LC	Nocturnal
Speothos venaticus	bush dog	들개	NT	Diurnal
Conepatus chinga	Molina's hog-nosed skunk	몰리나 돼지코 스컹크	LC	Nocturnal
Conepatus semistriatus	Striped hog-nosed skunk	줄무늬 돼지코 스컹크	LC	Nocturnal

Galictis cuja	lesser grison	작은 그리슨	LC	Diurnal
Galictis vittata	greater grison	큰 그리슨	LC	Diurnal
Eira barbara	tayra	타이라	LC	Diurnal
Mustela frenata	long-tailed weasel	긴꼬리 족제비	LC	Nocturnal
Bassaricyon alleni	eastern lowland olingo	동부저지대올링고	LC	Nocturnal
Leopardus guttulus	southern little spotted cat	남방호랑고양이	VU	Nocturnal
Leopardus tigrinus	nothern tiger cat	호랑고양이	VU	Nocturnal

Table S3-3. Carnivore species excluded

academic	common	korean	water	large_prey	Vegetarian (mainly fruit)
Lontra longicaudis	Neotropical otter	신열대구수달	1	0	0
Panthera onca	jaguar	재규어	0	1	0
Pteronura brasiliensis	Giant otter	큰수달	1	0	0
Puma concolor	puma	퓨마	0	1	0
Potos flavus	kinkajou	킨카주 너구리	0	0	1
Nasua nasua	south american coati	붉은 코코아티	0	0	1
Procyon cancrivorus	crab-eating raccon	게잡이 아메리카 너구리	1	0	0

Table S3-4. Avian species included

Family	academic	common	IUCN	Behaviors
Accipitridae	*Rupornis magnirostris*	Roadside Hawk	LC	Diurnal
Accipitridae	*Chondrohierax uncinatus*	Hook-billed Kite	LC	Diurnal
Accipitridae	*Parabuteo leucorrhous*	White-rumped Hawk	LC	Diurnal
Accipitridae	*Parabuteo unicinctus*	Harris's Hawk	LC	Diurnal
Accipitridae	*Pseudastur polionotus*	Mantled Hawk	NT	Diurnal
Accipitridae	*Circus buffoni*	Long-winged Harrier	LC	Diurnal
Accipitridae	*Spizaetus ornatus*	Ornate Hawk-eagle	NT	Diurnal
Accipitridae	*Spizaetus melanoleucus*	Black-and-white hawk-eagle	LC	Diurnal
Accipitridae	*Spizaetus tyrannus*	Black Hawk-eagle	LC	Diurnal
Accipitridae	*Gampsonyx swainsonii*	Pearl Kite	LC	Diurnal
Accipitridae	*Busarellus nigricollis*	Black-collared Hawk	LC	Diurnal
Accipitridae	*Buteogallus schistaceus*	Slate-colored Hawk	LC	Diurnal
Accipitridae	*Geranoaetus polyosoma*	Variable Hawk	LC	Diurnal
Accipitridae	*Buteogallus coronatus*	Crowned Solitary Eagle	EN	Diurnal
Accipitridae	*Geranospiza caerulescens*	Crane Hawk	LC	Diurnal
Accipitridae	*Buteogallus urubitinga*	Great Black Hawk	LC	Diurnal
Accipitridae	*Buteo albonotatus*	Zone-tailed hawk	LC	Diurnal
Accipitridae	*Geranoaetus albicaudatus*	White-tailed Hawk	LC	Diurnal

Accipitridae	*Buteo brachyurus*	Short-tailed Hawk	LC	Diurnal
Accipitridae	*Buteogallus lacernulatus*	White-necked Hawk	VU	Diurnal
Accipitridae	*Buteogallus meridionalis*	Savanna Hawk	LC	Diurnal
Accipitridae	*Geranoaetus melanoleucus*	Black-chested Buzzard-eagle	LC	Diurnal
Accipitridae	*Leptodon cayanensis*	Gray-headed kite	LC	Diurnal
Accipitridae	*Buteo nitidus*	Grey-lined Hawk	LC	Diurnal
Accipitridae	*Leucopternis kuhli*	White-browed Hawk	LC	Diurnal
Accipitridae	*Leucopternis melanops*	Black-faced Hawk	LC	Diurnal
Accipitridae	*Pseudastur albicollis*	White Hawk	LC	Diurnal
Accipitridae	*Harpia harpyja*	Harpy Eagle	NT	Diurnal
Accipitridae	*Harpagus bidentatus*	Double-toothed Kite	LC	Diurnal
Accipitridae	*Harpagus diodon*	Rufous-thighed Kite	LC	Diurnal
Accipitridae	*Morphnus guianensis*	Crested eagle	NT	Diurnal
Accipitridae	*Accipiter bicolor*	Bicolored hawk	LC	Diurnal
Accipitridae	*Accipiter striatus*	Sharp-shinned Hawk	LC	Diurnal
Accipitridae	*Accipiter poliogaster*	Gray-bellied hawk	NT	Diurnal
Accipitridae	*Ictinia plumbea*	Plumbeous kite	LC	Diurnal
Accipitridae	*Leptodon forbesi*	White-collared Kite	EN	Diurnal
Accipitridae	*Elanoides forficatus*	Swallow-tailed Kite	LC	Diurnal
Accipitridae	*Elanus leucurus*	White-tailed Kite	LC	Diurnal
Falconidae	*Micrastur mintoni*	Cryptic forest falcon	LC	Diurnal

Falconidae	*Micrastur mirandollei*	Slaty-backed Forest Falcon	LC	Diurnal
Falconidae	*Falco rufigularis*	Bat Falcon	LC	Diurnal
Falconidae	*Micrastur buckleyi*	Buckley's Forest-falcon	LC	Diurnal
Falconidae	*Micrastur gilvicollis*	Lined forest falcon	LC	Diurnal
Falconidae	*Falco deiroleucus*	Orange-breasted falcon	NT	Diurnal
Falconidae	*Micrastur ruficollis*	Barred Forest-falcon	LC	Diurnal
Falconidae	*Micrastur semitorquatus*	Collared Forest-falcon	LC	Diurnal
Falconidae	*Herpetotheres cachinnans*	Laughing Falcon	LC	Diurnal
Falconidae	*Falco sparverius*	American Kestrel	LC	Diurnal
Falconidae	*Falco femoralis*	Aplomado Falcon	LC	Diurnal
Falconidae	*Caracara cheriway*	Crested Caracara	LC	Diurnal
Falconidae	*Milvago chimachima*	Yellow-headed Caracara	LC	Diurnal
Falconidae	*Caracara plancus*	Southern Caracara	LC	Diurnal
Falconidae	*Ibycter americanus*	Red-throated Caracara	LC	Diurnal
Falconidae	*Daptrius ater*	Black Caracara	LC	Diurnal
Falconidae	*Phalcoboenus chimango*	Chimango Caracara	LC	Diurnal
Stirigidae	*Asio clamator*	Striped Owl	LC	Nocturnal
Stirigidae	*Asio flammeus*	Short-eared Owl	LC	Nocturnal
Stirigidae	*Asio stygius*	Stygian Owl	LC	Nocturnal
Stirigidae	*Athene cunicularia*	Burrowing Owl	LC	Nocturnal
Stirigidae	*Lophostrix cristata*	Crested Owl	LC	Nocturnal

Stirigidae	*Pulsatrix koeniswaldiana*	Tawny-browed Owl	LC	Nocturnal
Stirigidae	*Ciccaba huhula*	Black-banded Owl	LC	Nocturnal
Stirigidae	*Ciccaba virgata*	Mottled Owl	LC	Nocturnal
Stirigidae	*Bubo virginianus*	Great Horned Owl	LC	Nocturnal
Stirigidae	*Glaucidium minutissimum*	Least Pygmy-owl	LC	Nocturnal
Stirigidae	*Aegolius harrisii*	Buff-fronted Owl	LC	Nocturnal
Stirigidae	*Pulsatrix perspicillata*	Spectacled Owl	LC	Nocturnal
Stirigidae	*Strix hylophila*	Rusty-barred Owl	NT	Nocturnal
Stirigidae	*Megascops choliba*	Tropical Screech-owl	LC	Nocturnal
Stirigidae	*Megascops atricapilla*	Black-capped Screech-owl	LC	Nocturnal
Stirigidae	*Megascops sanctaecatarinae*	Long-tufted Screech-owl	LC	Nocturnal
Stirigidae	*Megascops vermiculatus*	Vermiculated Screech-owl	LC	Nocturnal
Stirigidae	*Megascops watsonii*	Tawny-bellied Screech-owl	LC	Nocturnal
Stirigidae	*Glaucidium brasilianum*	Ferruginous Pygmy-owl	LC	Nocturnal
Stirigidae	*Glaucidium hardyi*	Amazonian Pygmy-owl	LC	Nocturnal
Stirigidae	*Glaucidium mooreorum*	Pernambuco Pygmy-owl	CR	Nocturnal

Table S3-5. Avian species excluded

Family	academic	common	Water	Small predator
Accipitridae	*Rostrhamus sociabilis*	Snail kite	O	
Accipitridae	*Buteogallus aequinoctialis*	Rufous Crab-hawk	O	
Accipitridae	*Accipiter superciliosus*	Tiny Hawk		O
Accipitridae	*Helicolestes hamatus*	Slender-billed Kite	O	

Appendix 3-3. Co-distribution of each reservoir rodent with *N. lasiurus*

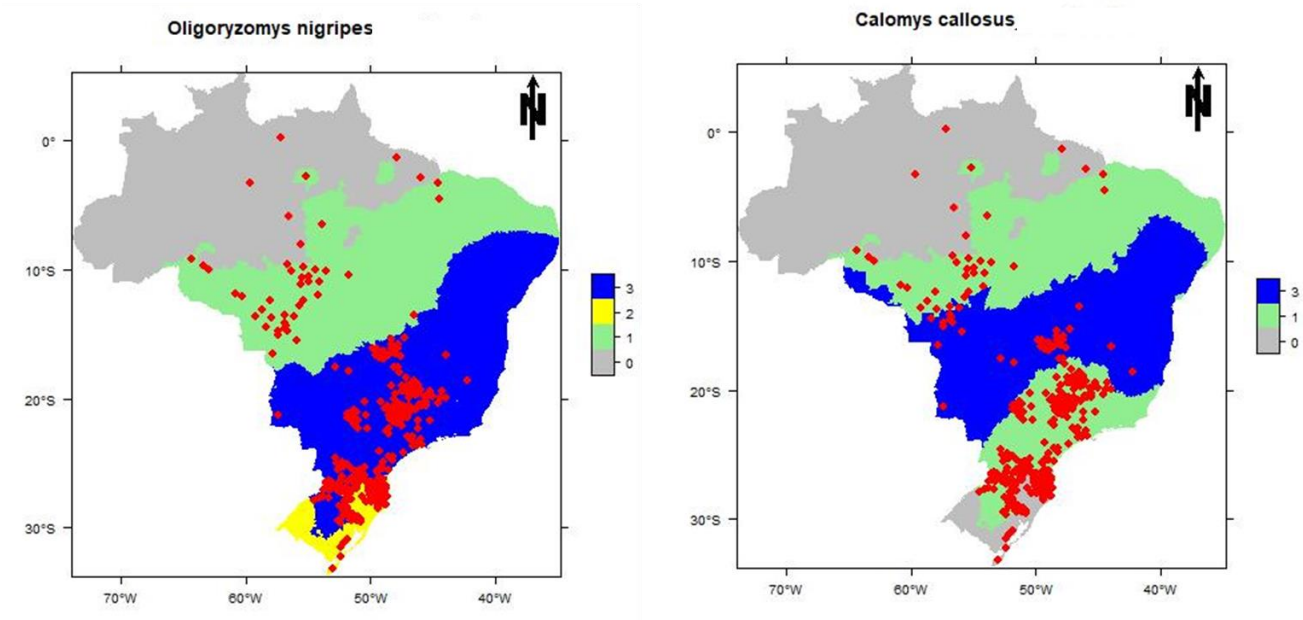


Figure S3-1. Joint distribution of *Necromys lasiurus* with *Oligoryzomys nigripes* (left) and *Calomys callosus* (right)

Note: Blue indicates that regions with co-existence, and regions with yellow color represent area with each reservoir and absence of *N. lasiurus*. Green area indicates presence of *N. lasiurus* without each reservoir and grey area showed absence of the two reservoirs

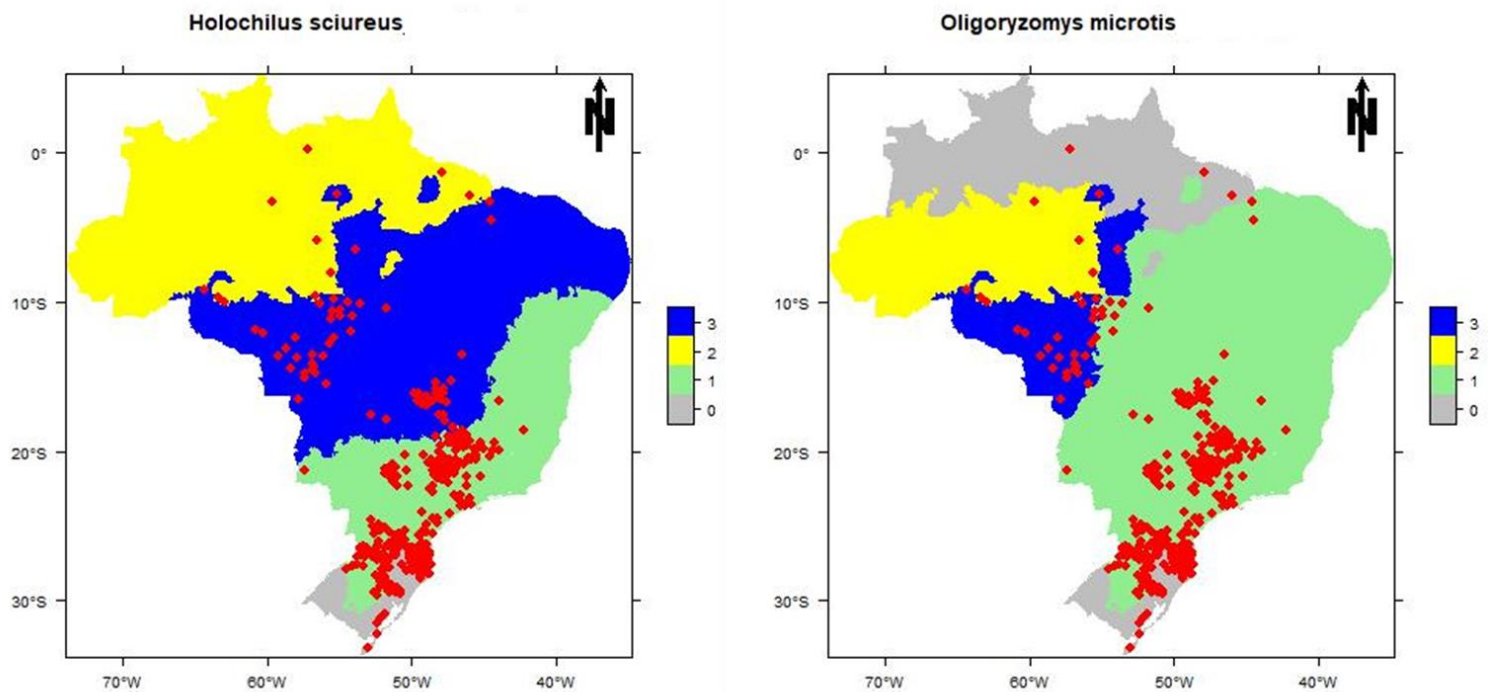


Figure S3-2. Joint distribution of *Necromys lasiurus* with *Holochilus sciureus* (left) and *Oligoryzomys microtis* (right)

Note: Blue indicates that regions with co-existence, and regions with yellow color represent area with each reservoir and absence of *N. lasiurus*. Green area indicates presence of *N. lasiurus* without each reservoir and grey area showed absence of the two reservoirs

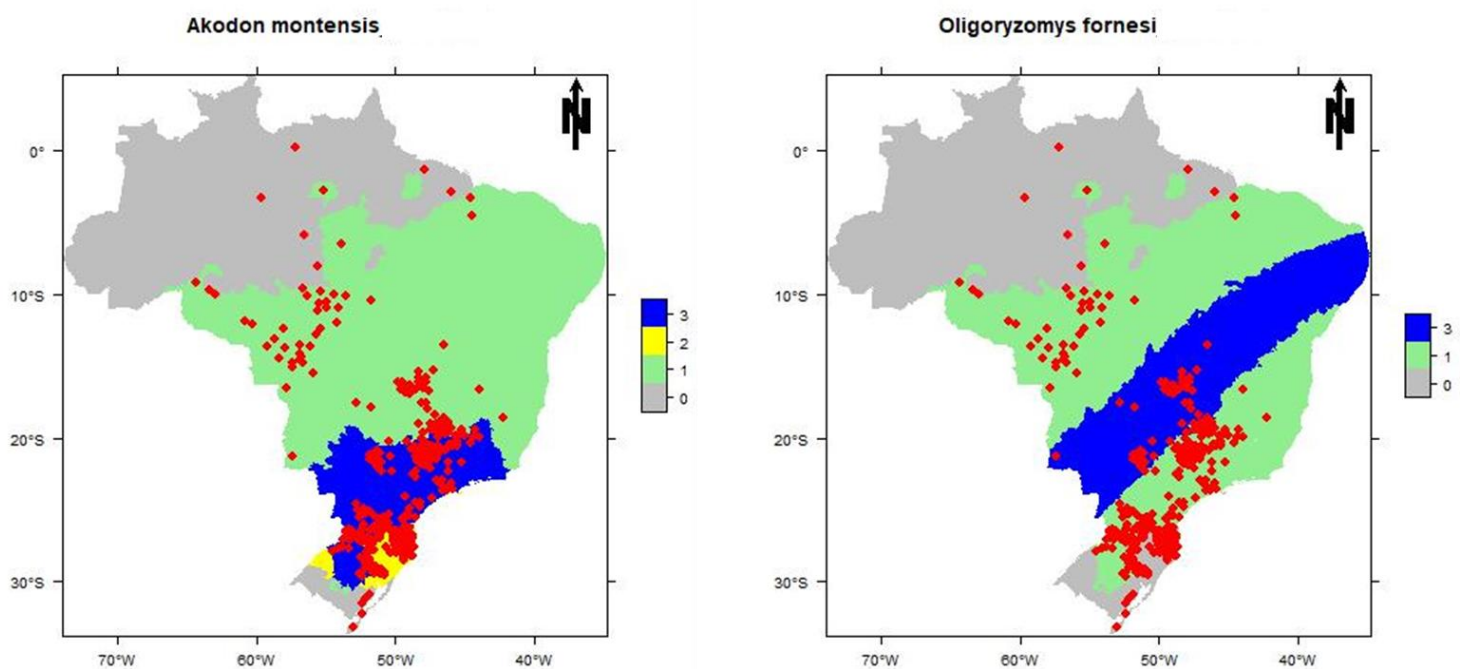


Figure S3-3. Joint distribution of *Necromys lasiurus* with *Akodon montensis* (left) and *Oligoryzomys fornesi* (right)

Note: Blue indicates that regions with co-existence, and regions with yellow color represent area with each reservoir and absence of *N. lasiurus*. Green area indicates presence of *N. lasiurus* without each reservoir and grey area showed absence of the two reservoirs

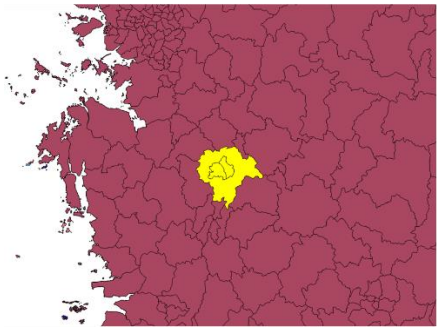
Appendix 4-1. Standardization of Korean administrative region

Step 1. Figure out changes on administrative region in South Korea

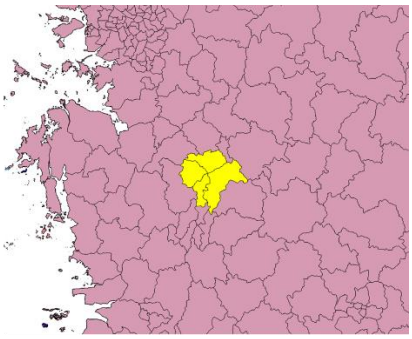
Table S4-1. Changes of administrative regions in South Korea

ID	Year	Sigungu (Korean)	Type of changes
1	2013	청주시	Complex
2	2003	수원시	Complex
3	2009	마산, 창원, 진해	Converging
4	2004	용인시	Divide
5	2004	일산구	Divide
6	2005	제주시	Converging
7	2015	부천시	Converging
8	2007	천안시	Divide
9	2002	안산시	Divide

#1 청주시

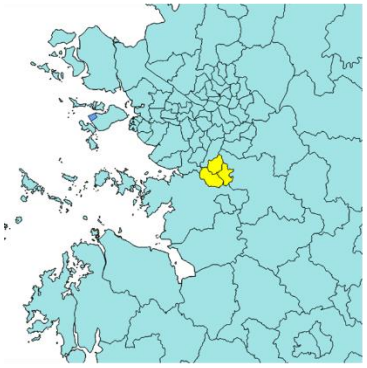


2013

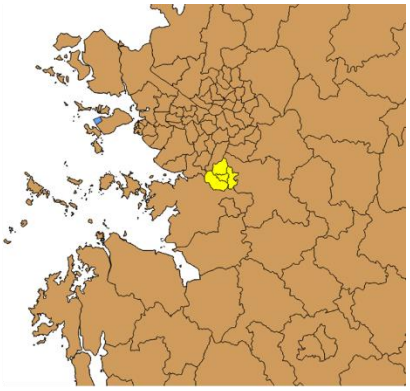


2014

#2 수원시

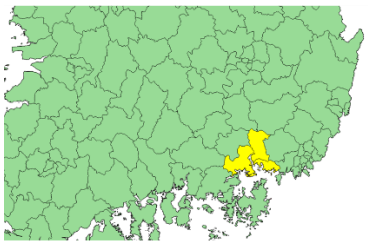


2003

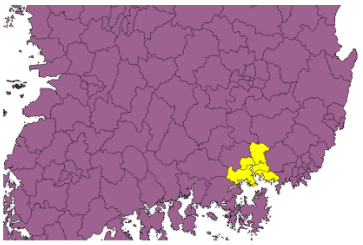


2004

#3 마산, 창원, 진해

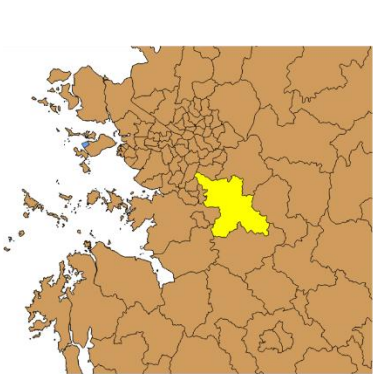


2009

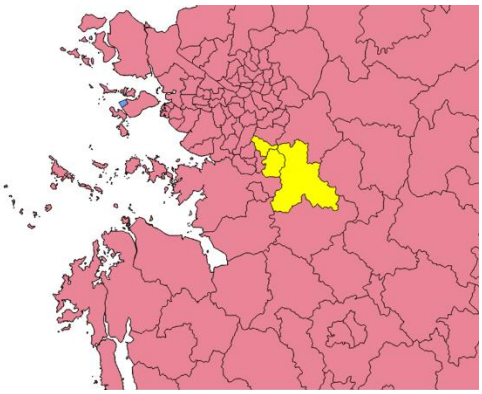


2010

#4 용인시

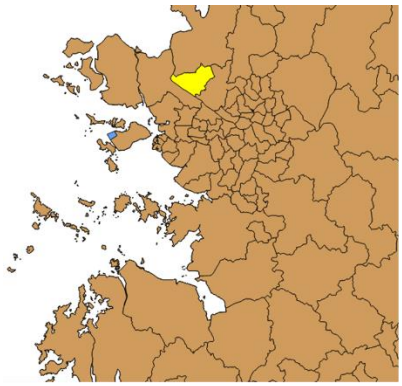


2004

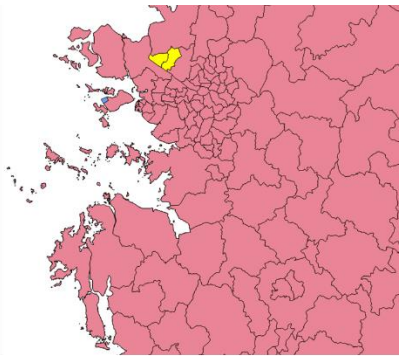


2005

#5 일산구



2004



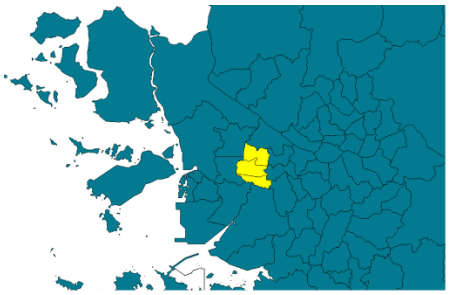
2005

#6 제주시

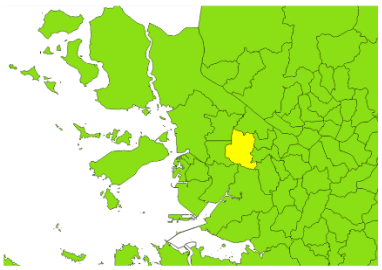
2005

2006

#7 부천시

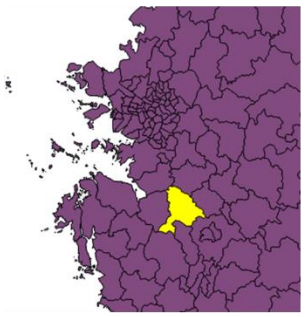


2015

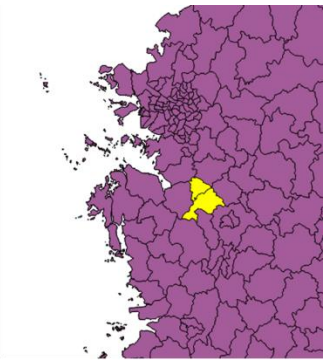


2016

#8 천안시

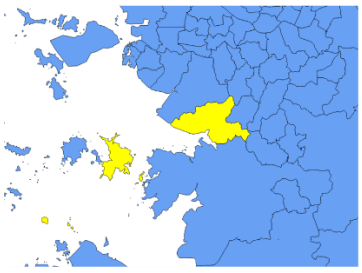


2007

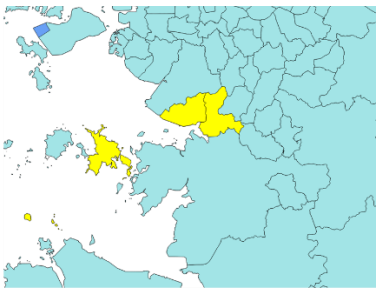


2008

#9 안산시



2002



2003

Appendix 4-2. Species included to count species richness in South Korea

Table S4-2. Carnivore species included

academic	common	Korean	IUCN	behavior
Meles leucurus	badger	오소리	NT	Nocturnal
Mustela sibirica	weasel	족제비	LC	Nocturnal
Mustela nivalis	Manchurian weasel	무산쇠족제비	VU	Cathemeal
Martes flavigula	marten	담비	VU	Diurnal
Lutra lutra	otter	수달	VU	Nocturnal
Nyctereutes procyonoides	raccoon dog	너구리	LC	Nocturnal
Prionailurus bengalensis	Leopard Cat	삵	VU	Nocturnal

Table S4-3. Avian species included

academic	Korean	IUCN	behavior
Accipiter gularis	조롱이	VU	Diurnal
Accipiter nisus	새매	VU	Diurnal
Accipiter gentilis	참매	VU	Diurnal
Butastur indicus	왕새매	LC	Diurnal
Buteo buteo	말똥가리	LC	Diurnal
Buteo hemilasius	큰말똥가리	LC	Diurnal
Buteo lagopus	털발말똥가리	LC	Diurnal
Aquila chrysaetos	검독수리	EN	Diurnal
Accipiter soloensis	붉은배새매	VU	Diurnal
Circus melanoleucos	알락개구리매	LC	Diurnal
Milvus migrans	솔개	VU	Diurnal
Haliaeetus albicilla	흰꼬리수리	VU	Diurnal
Haliaeetus pelagicus pelagicus	참수리	EN	Diurnal
Circus spilonotus	개구리매	LC	Diurnal
Circus cyaneus	잿빛개구리매	LC	Diurnal
Falco tinnunculus	황조롱이	LC	Diurnal

Falco amurensis	비둘기조롱이	NT	Diurnal
Falco columbarius	쇠황조롱이	NT	Diurnal
Falco peregrinus	매	VU	Diurnal
Athene noctua	금눈쇠올빼미	LC	Nocturnal
Asio flammeus	쇠부엉이	LC	Nocturnal
Strix aluco	올빼미	VU	Nocturnal
Bubo bubo	수리부엉이	VU	Nocturnal
Otus bakkamoena	큰소쩍새	LC	Nocturnal

국문 초록

포식동물 종 풍부도가 설치류매개 감염병 출현과 발생에 미치는 영향

민경덕

서울대학교 보건대학원 보건학과 보건학전공

설치류는 전세계에 널리 분포하고 있으며, 전체 육상 포유류의 40%에 해당할 정도로 번성한 종이다. 주로 먹이사슬의 하위에 위치하여 생태계의 먹이사슬을 유지하는데 중요한 위치에 있기도 하다. 환경에 대한 적응력이 뛰어나 인간의 거주지 영역에서도 번식 및 생활이 잘 이루어지는 편인데, 이러한 특성으로 인하여 인간의 감염병을 매개하는 병원체 보유숙주로서, 오래전부터(예: 중세시대 흑사병) 위협이 되고 있는 존재이기도 하다. 최근에도 설치류 매개질병은 라싸열, 흑사병 등 출현 재출현 감염병과 한타바이러스 감염증(유행성 출혈열) 등의 상재 감염병, 렙토스피라 감염증과 같은 자연재해 상황에서 발생하는 질병에 이르기까지 다양한 형태로 보건학적, 사회경제적 피해를 일으키고 있다. 이에 여러 연구에서 설치류매개감염병의 위험요인을 찾아내고, 이를 실질적 중재 혹은 예측에 활용하고자 하는 학문적 정책적 노력들이 지속되고 있다. 주로 개인수준의 요인, 인구사회학적 요인, 혹은 기후, 지리적요인과 같은 무생물적 환경요인(abiotic environmental factor)에 대한 연구가 대부분을

차지하며, 상대적으로 야생동물 요인 즉, 생태계 내 포식자들의 역할 혹은 먹이경쟁종의 역할에 대한 연구는 부족한 상태이다.

포식동물들의 역할 혹은 먹이경쟁종의 역할에 대한 연구를 위해서 다음의 두가지 접근법이 있다. 첫째는 각 야생동물들의 개체수를 측정하거나 기존에 측정된 자료를 활용한 연구이며, 둘째는 포식동물들의 종 풍부도(species richness) 즉 얼마나 많은 종이 있는지에 대한 자료를 수집하여 수행하는 연구이다. 두가지 방법 모두 가능하며, 첫번째 접근법의 경우 보다 직관적으로 야생동물들의 영향을 파악할 수 있다는 장점이 있지만, 각각의 개체수를 측정하는 것이 현재의 기술로 매우 어려울 뿐만 아니라, 계절 등 환경적 변화에 따라 크게 바뀔 수 있기 때문에 실질적으로 연구를 수행하기 어려운 측면이 있다. 또한 질병발생의 위험요인을 규명하는 연구의 목표중 하나가 질병발생의 예측에 활용한다는 점인 것을 감안하였을때, 측정이 어려운 지표는 예측인자로서의 활용도도 낮다고 할 수 있다. 반면 종 풍부도의 경우, 상대적으로 측정이 용이 하기 때문에 앞서 기술한 두가지의 어려움을 극복할 수 있는 지표로 생각할 수 있다. 또한 기존의 생태학적 연구를 통해 개체수와는 별개로 야생동물의 종 풍부도가 보유숙주 설치류의 생태에 영향을 준다는 것도 지속적으로 보고되고 있다. 예를 들어 포식동물의 종 풍부도가 증가하면 피식종(prey species)의 활동성이 떨어진다는 연구결과와 설치류의 종 풍부도가 증가하면 설치류들의 활동성이 낮아진다는 연구결과들이 있다.

이에 본 연구에서는 포식동물 및 설치류의 종 풍부도가 높은 지역에서는 낮은 지역에 비해 매개 설치류의 활동성이 낮기 때문에 인간집단에서의 설치류매개질병 전파 위험도가 낮은 것이라는 가설을 상정하였다. 이 가설과 관련하여 기존 연구들을 고찰해보면, 설치류 종 풍부도와 사람에서 질병발생과 관련해서는 질병생태학 분야에서 다수의 논문들이 발표되었지만, 그 효과에 대해서는 명확한 결론이 나지 않은 상황이다. 즉 설치류 종 풍부도, 혹은 다양성이 높은 지역에서 사람에서 질병발생위험이 더 높다는 주장(amplification effect)과 앞서 기술한 것처럼 사람에서의 질병발생위험을 줄인다는 주장(dilution effect, 희석효과)이

아직까지도 대립되고 있는 상황이다. 한편 포식동물 다양성의 영향에 대해서는 거의 연구된 바가 없는 것을 확인할 수 있었는데, 2011 년에 Orrock 등이 채널제도(Channel islands)의 8 개 섬을 대상으로한 연구에서 포식동물 종 풍부도가 설치류의 한타바이러스 감염증 유병률에 방어작용을 한다는 보고를 한 것이 유일한 연구이다. 그러나 이 연구도 표본수가 낮았다는 점(N=8), 섬 지역을 대상으로하여 육상지역에서의 상황을 반영할 수 없다는 점, 그리고 인간집단에서의 질병발생의 영향을 보지 않았다는 점에서 추가적인 연구가 필요한 상황이라고 할 수 있다.

이러한 배경에서 본 연구를 계획하게 되었다. 결과의 해석력을 높이기 위해서 진드기, 모기등 다른 매개체(vector)가 전파에 있어 필요하지 않는 라싸열, 한타바이러스감염증을 연구 대상질병으로 하였으며, 결과의 일반화를 위해 다양한 생태학적 맥락(ecological context), 즉 3 개의 이질적인 지역(서아프리카지역, 브라질, 한국)을 연구대상지역으로 하였다. 또한 혼란요인으로 부터 오는 Bias 를 최소화하기 위해 기존 연구를 참고하여, 종풍부도(주 설명변수)와 사람에서의 설치류매개 감염병 발생(결과변수)에 모두 영향을 주는 것으로 보고된 사회경제적요인, 지리적요인, 토지이용, 기후요인을 보정하였다. (Table A-1)

첫번째 연구는 서아프리카 지역의 라싸열(Lassa fever)에 대한 연구로서, 2006 년이전까지의 라싸열이 발생하지 않았던 지역 중 2006 년 이후 라싸열이 발생한 지역(새롭게 라싸열이 출현한 지역)과 나머지 지역의 차이가 포식동물의 종 풍부도와 상관성이 있는지를 조사하였다. 라싸열의 매개종은 다유방쥐 (Mastomys natalensis)로서 야행성인데, 연구 결과 포식동물의 종 풍부도는 통계적으로 유의한 상관성을 나타내지 않았고 반면에 설치류의 종 풍부도가 높은 지역에서는 라싸열 출현의 확률이 낮은 것으로 나타났다. (Table A-2)

두번째 연구는 브라질에서의 한타바이러스 감염증(New world hantavirosis; hantavirus pulmonary syndrome)에 대한 연구로서, 2007 년부터 2014 년까지 한타바이러스 감염벙이 보고된 지역(municipality level)과 보고되지 않은 지역의 차이가 포식동물의 종 풍부도와 상관성이 있는지를

살펴보았다. 연구 결과 주행성 일주기를 나타내는 포식종의 풍부도가 높은 지역에서 한타바이러스 감염증의 발생 보고 확률이 낮은 것으로 나타났고, 반대로 야행성 포식동물의 풍부도가 높은지역에서는 한타바이러스 감염증의 발생 보고 확률이 높은 것을 확인할 수 있었다. (Table A-2)

세번째 연구에서는 한국의 유행성출혈열(Old world hantavirosis; hemorrhagic fever with renal syndrome)에 대한 연구로서, 2006 년부터 2016 년까지 질병관리본부에 보고된 시군구별 유행성 출혈열의 발생건수와 포식동물의 종풍부도가 상관성이 있는지를 보고자 하였다. 연구결과 주행성 포식동물의 풍부도가 높은 지역에서 유행성출혈열 발생건수의 상대위험도가 높은 것으로 나타났으며, 야행성 포식동물의 종 풍부도와는 통계적으로 유의한 상관성을 확인할 수 없었다. (Table A-2)

각 연구는 공개된 자료를 활용한 생태학적 연구로서 여러 한계점을 지니고 있어 해석에 주의가 필요하지만, 매개 설치류종이 우점종인 지역(브라질, 한국)에서는 그 매개종과 일주기가 동일한 포식동물의 종풍부도는 매개감염병의 출현과 발생에 있어 음의 상관관계가 나타났다는 점은 본 연구 서두에서 제기했던 가설, 즉 포식동물의 종 풍부도가 설치류매개감염병의 조절작용을 한다는 주장을 강력하게 뒷받침한다고 볼 수 있다. 본 연구를 통해 나타난 상관성의 크기는 높지 않지만, 만약 위 주장이 이후의 연구를 통해 받아들여지게 된다면 이는 포식동물의 종풍부도가 본 연구에서 대상으로 삼은 라싸열, 한타바이러스감염증 뿐만아니라 다른 모든 설치류매개감염병에도 동일하게 적용될수 있다는 점을 시사하며, 보건학 뿐만 아니라 야생동물 보전분야에 있어서도 의미하는 바가 크다고 할 수 있다.

주요어: 포식동물, 종 풍부도, 설치류 매개 감염병, 신종감염병, 원헬스

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